Refine Search

Search Results -

Term	Documents
LIPFORD-G$-B$	0
LIPFORD-GRAYSON-B	3
LIPFORD-GRAYSON-B-DR	1
LIPFORD-G-B	4
LIPFORD-G$-B$.IN..PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	8
(LIPFORD-G$-B$.IN.).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	8

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L10

Refine Search | Recall Text | Clear | Interrupt

Search History

DATE: Friday, March 19, 2004 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=AND			
L10	Lipford-G$-B$.in.	8	L10
L9	L8 not L7	37	L9
L8	L6 and (dendritic or pDC2)	61	L8
L7	L6 and (interferon adj alpha)	29	L7
L6	L5 or L4	134	L6

h e b b cg b e e ch

L5	(ODN adj 1585)	14	L5
L4	(CpG) same ((poly-G) or (poly(G)))	133	L4
L3	L1 and L2	2	L3
L2	Krieg-arthur-M$.in.	38	L2
L1	Hartmann-Gunther.in.	23	L1

END OF SEARCH HISTORY

PALM INTRANET

Day : Friday
Date: 3/19/2004

Time: 14:59:25

Inventor Name Search

Enter the **first few letters** of the Inventor's Last Name.
Additionally, enter the **first few letters** of the Inventor's First name.

Last Name	**First Name**	
Hartmann	Gunther	Search

To go back use Back button on your browser toolbar.

Back to PALM | ASSIGNMENT | OASIS | Home page

h e eb cg b e f e

Status: Path 1 of [Dialog Information Services via Modem]

Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
******** HHHHHHHH SSSSSSSS?
Status: Signing onto Dialog
****
ENTER PASSWORD:
******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
Status: Connected

Dialog level 04.01.00D

Last logoff: 16mar04 15:05:59
Logon file001 19mar04 16:32:27
*** ANNOUNCEMENT ***
***
--File 654 - US published applications from March 15, 2001 to the present are now online. Please see HELP NEWS 654 for details.

***
--File 581 - The 2003 annual reload of Population Demographics is complete. Please see Help News581 for details.

***
--File 990 - NewsRoom now contains February 2003 to current records.
File 992 - NewsRoom 2003 archive has been newly created and contains records from January 2003. The oldest months's records roll out of File 990 and into File 992 on the first weekend of each month.
To search all 2003 records BEGIN 990, 992, or B NEWS2003, a new OneSearch category.
***
--Connect Time joins DialUnits as pricing options on Dialog.
See HELP CONNECT for information.
***
***
--SourceOne patents are now delivered to your email inbox as PDF replacing TIFF delivery. See HELP SOURCE1 for more information.
***
--Important news for public and academic libraries. See HELP LIBRARY for more information.
***
--Important Notice to Freelance Authors--
See HELP FREELANCE for more information
***
NEW FILES RELEASED
***DIOGENES: Adverse Drug Events Database (File 181)
***World News Connection (File 985)
***Dialog NewsRoom - 2003 Archive (File 992)
***TRADEMARKSCAN-Czech Republic (File 680)
***TRADEMARKSCAN-Hungary (File 681)
***TRADEMARKSCAN-Poland (File 682)
***
UPDATING RESUMED
***
RELOADED
***Medline (Files 154-155)
***Population Demographics -(File 581)
***CLAIMS Citation (Files 220-222)

REMOVED
***

>>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
>>> of new databases, price changes, etc. <<<
****
KWIC is set to 50.
HILIGHT set on as '*'
*
*
* ALL NEW CURRENT YEAR RANGES HAVE BEEN * * *
* * * INSTALLED * * *

File 1:ERIC 1966-2004/Mar 11
(c) format only 2004 The Dialog Corporation

Set Items Description
--- ----- -----------
Cost is in DialUnits
?b 155, 159
19mar04 16:32:34 User259876 Session D601.1
$0.32 0.090 DialUnits File1
$0.32 Estimated cost File1
$0.03 TELNET
$0.35 Estimated cost this search
$0.35 Estimated total session cost 0.090 DialUnits

SYSTEM:OS - DIALOG OneSearch
File 155:MEDLINE(R) 1966-2004/Mar W2
(c) format only 2004 The Dialog Corp.
***File 155: Medline has been reloaded. Accession numbers**
have changed. Please see HELP NEWS 154 for details.
File 159:Cancerlit 1975-2002/Oct
(c) format only 2002 Dialog Corporation
***File 159: Cancerlit ceases updating with immediate effect.**
Please see HELP NEWS.

Set Items Description
--- ----- -----------
?s (CpG or CG) (s) (polyG or poly-G or (poly(G))
>>>Unmatched parentheses
?s (CpG or CG) (s) (polyG or poly-G or poly(G))
8673 CPG
5422 CG
33 POLYG
0 POLY-G
0 POLY(G)
S1 1 (CPG OR CG) (S) (POLYG OR POLY-G OR POLY(G))
?t s1/3,k/all

1/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

11952537 PMID: 12162698
Antitumor mechanisms of oligodeoxynucleotides with *CpG* and *polyG* motifs in murine prostate cancer cells: decrease of NF-kappaB and AP-1 binding activities and induction of apoptosis.
Shen Weiyin; Waldschmidt Marianella; Zhao Xiuqin; Ratliff Timothy; Krieg Arthur M
Department of Internal Medicine, University of Iowa, Iowa City 52242, USA.
Antisense & nucleic acid drug development (United States) Jun 2002, 12 (3) p155-64, ISSN 1087-2906 Journal Code: 9606142
Contract/Grant No.: CA66570; CA; NCI; DK25295; DK; NIDDK; DK54759; DK; NIDDK

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Antitumor mechanisms of oligodeoxynucleotides with *CpG* and *polyG* motifs in murine prostate cancer cells: decrease of NF-kappaB and AP-1 binding activities and induction of apoptosis.

Previous studies have shown that *CpG* oligodeoxynucleotides (ODNs) have substantial immunostimulatory effects with anticancer applications. The antitumor applications that have been described previously are mediated through the *CpG*-induced activation of the host immune system, not through direct antitumor effects. Using cytostasis and cell proliferation assays, we demonstrated that specific ODNs inhibit the...

... and NF-kappaB in a time-dependent manner. Evaluation of a panel of ODNs containing different DNA motifs demonstrated that the optimal proapoptotic sequences required *polyG* sequences but that *CpG* motifs were not essential. Finally, in vivo antitumor studies showed that the proapoptotic *polyG* motifs significantly inhibited prostate tumor growth. *PolyG* motifs inhibited tumor growth, and the effects were enhanced by *CpG* immune activating sequences. ODN containing both *polyG* and *CpG* motifs may have enhanced efficacy in tumor therapy through multiple mechanisms of action, including direct antitumor activities and immune activation.

?ds

```
Set     Items   Description
S1          1   (CPG OR CG) (S) (POLYG OR POLY-G OR POLY(G))
?s (ODN (w) 1585)
          2370  ODN
           205  1585
      S2     6  (ODN (W) 1585)
?s s2 and (pDC2 or dendritic)
             6  S2
            39  PDC2
         36510  DENDRITIC
      S3     0  S2 AND (PDC2 OR DENDRITIC)
?rd s2
...completed examining records
      S4     3  RD S2 (unique items)
?t s4/3,k/all
```

4/3,K/1 (Item 1 from file: 155)

11507547 PMID: 11673492

Divergent therapeutic and immunologic effects of oligodeoxynucleotides with distinct CpG motifs.

Ballas Z K; Krieg A M; Warren T; Rasmussen W; Davis H L; Waldschmidt M; Weiner G J

Department of Veterans Affairs Medical Center, Iowa City, IA 52246, USA. ballasz@uiowa.edu

Journal of immunology (Baltimore, Md. - 1950) (United States) Nov 1 2001, 167 (9) p4878-86, ISSN 0022-1767 Journal Code: 2985117R

Contract/Grant No.: DK25295; DK; NIDDK; P01 CA66570; CA; NCI; R01 CA77764 ; CA; NCI; T32 HL07344; HL; NHLBI

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... tails, is a potent inducer of NK lytic activity but has little effect on cytokine secretion or B cell proliferation. One such NK-optimized CpG *ODN* (*1585*) can induce regression of established melanomas in mice. Surprisingly, no such therapeutic effects were seen with CpG ODN optimized for activation of B cells and...

4/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11398520 PMID: 11493473
Synthetic unmethylated cytosine-phosphate-guanosine oligodeoxynucleotides are potent stimulators of antileukemia responses in naive and bone marrow transplant recipients.
Blazar B R; Krieg A M; Taylor P A
University of Minnesota Cancer Center, Minneapolis, MN, USA.
Blood (United States) Aug 15 2001, 98 (4) p1217-25, ISSN 0006-4971 Journal Code: 7603509
Contract/Grant No.: P01 CA66579; CA; NCI; R01 CA-72669; CA; NCI; R01 HL63452; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... oligodeoxynucleotides (ODNs) can induce relatively more B-cell activation or relatively more natural killer (NK)--cell activation. To evaluate their antitumor activities, an NK-optimized *ODN* (*1585*) and 2 B-cell--optimized ODNs (1826 and 2006) were compared for their ability to protect naive mice against a lethal acute myelogenous leukemia (AML...

4/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11183091 PMID: 11179339
Interleukin-12- and gamma interferon-dependent protection against malaria conferred by CpG oligodeoxynucleotide in mice.
Gramzinski R A; Doolan D L; Sedegah M; Davis H L; Krieg A M; Hoffman S L
Malaria Program, Naval Medical Research Center, Silver Spring, Maryland 20910-7500, USA.
Infection and immunity (United States) Mar 2001, 69 (3) p1643-9, ISSN 0019-9567 Journal Code: 0246127
Erratum in Infect Immun 2002 Sep;70(9) 5338
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... challenge with Plasmodium yoelii sporozoites conferred sterile protection against infection. A higher level of protection was consistently induced by CpG ODN 1826 compared with CpG *ODN* *1585*. The protective effects of both CpG ODNs were dependent on interleukin-12, as well as IFN-gamma. Moreover, CD8+ T cells (but not CD4+ T cells), NK cells, and nitric oxide were implicated in the CpG *ODN* *1585*-induced protection. These data establish that the protective mechanism induced by administration of CpG *ODN* *1585* in the absence of parasite antigen is similar in nature to the mechanism induced by immunization with radiation-attenuated P. yoelii sporozoites or with plasmid...
Chemical Name: Adjuvants, Immunologic; CpG *ODN* *1585*; CpG ODN 1826; Thionucleotides; Nitric Oxide; Interleukin-12; Interferon Type II; DNA
?ds

Set	Items	Description
S1	1	(CPG OR CG) (S) (POLYG OR POLY-G OR POLY(G))
S2	6	(ODN (W) 1585)
S3	0	S2 AND (PDC2 OR DENDRITIC)
S4	3	RD S2 (unique items)

?s (dendritic or pDC2s or IPCs) and (CpG or (ODN (w) 1585))
36510 DENDRITIC

```
              2  PDC2S
            221  IPCS
           8673  CPG
           2370  ODN
            205  1585
              6  ODN(W)1585
      S5      277  (DENDRITIC OR PDC2S OR IPCS) AND (CPG OR (ODN (W) 1585))
?s s5 and (poly(G))
            277  S5
              0  POLY(G)
      S6      0  S5 AND (POLY(G))
?s s5 not py>2000
            277  S5
        1843573  PY>2000
      S7     77  S5 NOT PY>2000
?rd
...examined 50 records  (50)
...completed examining records
      S8     48  RD (unique items)
?s s8 and (interferon)
             48  S8
         144289  INTERFERON
      S9      7  S8 AND (INTERFERON)
?rd
...completed examining records
     S10      7  RD (unique items)
?t s10/3,k/all
```

10/3,K/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

14429574 PMID: 10427997

Oligodeoxynucleotides containing *CpG* motifs induce IL-12, IL-18 and IFN-gamma production in cells from allergic individuals and inhibit IgE synthesis in vitro.

Bohle B; Jahn-Schmid B; Maurer D; Kraft D; Ebner C

Department of General and Experimental Pathology, University of Vienna, Austria.

European journal of immunology (GERMANY) Jul 1999, 29 (7) p2344-53, ISSN 0014-2980 Journal Code: 1273201

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Oligodeoxynucleotides containing *CpG* motifs induce IL-12, IL-18 and IFN-gamma production in cells from allergic individuals and inhibit IgE synthesis in vitro.

The effects of phosphorothioate oligonucleotides containing *CpG* motifs (*CpG* -ODN) on cultured cells from allergic patients and non-atopic individuals were investigated. In peripheral blood mononuclear cells (PBMC) *CpG* -ODN led to a significant increase of IFN-gamma. By intracellular cytokine staining, IFN-gamma production could be attributed to NK cells and inhibition experiments indicated an IL-12-dependent mechanism. Moreover, *CpG* -ODN increased mRNA expression of IL-12 and IL-18 in PBMC. In this respect, no significant difference between allergic and non-atopic individuals was observed. Monocyte-derived *dendritic* cells were identified as one IL-12- and IL-18-producing source. In addition, stimulation of PBMC derived from atopic patients with *CpG*-ODN led to a considerable increase of polyclonal IgG and IgM synthesis. In contrast, the production of total IgE was suppressed. *CpG*-ODN induced a significant rise of IgG and IgM specific for allergens to which the patients were sensitized, whereas allergen-specific IgE levels remained unchanged. Our data suggest that *CpG* -ODN display a strong influence on the ongoing immune response and might represent potential adjuvants for specific immunotherapy of type I allergy.

Descriptors: Hay Fever--immunology--IM; *Immunoglobulin E--biosynthesis --BI; **Interferon* Type II--biosynthesis--BI; *Interleukin-12 --biosynthesis--BI; *Interleukin-18--biosynthesis--BI; *Oligodeoxyribonucle otides--genetics--GE; *Oligodeoxyribonucleotides--pharmacology--PD; Base Sequence; *CpG* Islands; Hay Fever--genetics--GE; Immunoglobulin G --biosynthesis--BI; Immunoglobulin M--biosynthesis--BI; Interleukin-12 --genetics--GE; Interleukin-18--genetics--GE; Killer Cells, Natural --immunology...

Chemical Name: Immunoglobulin G; Immunoglobulin M; Interleukin-18; Oligodeoxyribonucleotides; RNA, Messenger; Thionucleotides; Interleukin-12; Immunoglobulin E; *Interferon* Type II

10/3,K/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

12486093 PMID: 12937643

Immunotherapeutic applications of *CpG*-containing oligodeoxynucleotides.

Klinman D M; Ishii K J; Gursel M; Gursel I; Takeshita S; Takeshita F

Section of Retroviral Research, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, Maryland 20892, USA.

Drug news & perspectives (Spain) Jun 2000, 13 (5) p289-96, ISSN 0214-0934 Journal Code: 8809164

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: PubMed not MEDLINE

Immunotherapeutic applications of *CpG*-containing oligodeoxynucleotides.

Bacterial DNA and synthetic oligodeoxynucleotides (ODN) expressing unmethylated *CpG* motifs stimulate the mammalian immune system to mount a rapid innate immune response. This response is characterized by the production of polyreactive IgM, immunomodulatory cytokines and chemokines. *CpG* ODN directly stimulate lymphocytes, natural killer cells and professional antigen-presenting cells (such as macrophages and *dendritic* cells). Owing to the strength and nature of this stimulation, *CpG* ODN are being harnessed for a variety of therapeutic uses. They are being tested for their ability to act as immune adjuvants, boosting the immune response elicited by conventional and DNA vaccines. As a result of their ability to activate a strong *interferon* gamma-dominated Th1 response while blocking the development of Th2-dependent allergies, *CpG* ODN are being examined for their antiallergic properties. Finally, *CpG* ODN are being used as "immunoprotective agents", since the innate immune response they elicit can protect the host from a variety of pathogenic bacteria, viruses...

10/3,K/3 (Item 3 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10879456 PMID: 11012752

Poly-guanosine motifs costimulate antigen-reactive CD8 T cells while bacterial *CpG* -DNA affect T-cell activation via antigen-presenting cell-derived cytokines.

Lipford G B; Bendigs S; Heeg K; Wagner H

Institute of Medical Microbiology, Immunology and Hygiene, Technical University of Munich, Munich, Germany.

Immunology (ENGLAND) Sep 2000, 101 (1) p46-52, ISSN 0019-2805 Journal Code: 0374672

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Poly-guanosine motifs costimulate antigen-reactive CD8 T cells while

bacterial *CpG* -DNA affect T-cell activation via antigen-presenting cell-derived cytokines.

Pathogen-derived pattern recognition ligands like lipopolysaccharide (LPS) and bacterial cytidine-guanosine (*CpG*)-DNA not only activate *dendritic* cells and macrophages but are also mitogenic for B cells. Less clear are the claimed effects of *CpG*-DNA on T cells, which range from direct activation, costimulation, or indirect transient activation via antigen-presenting cell (APC)-derived *interferon* type I (IFN type I). Here we demonstrate that *CpG* -DNA sequence specifically triggers macrophages to produce IFN type I, interleukin (IL)-12, IL-6 and tumour necrosis factor (TNF), but lacks the ability to directly costimulate T cells. Strikingly, poly-guanosine (poly-G) extensions to *CpG*-containing oligonucleotides (ODN) abolished the macrophage stimulatory potential yet generated T-cell costimulatory activities. In fact, independently of *CpG* -motifs, poly-G-ODN displayed the ability to costimulate T cells. Costimulation was operative on CD8 T cells but not CD4 T cells. Poly-G...

...2-driven T-cell proliferation and induced cytolytic T cells. Overall the data imply that poly-G motifs costimulate antigen reactive CD8 T cells, while *CpG* -DNA motifs fail to do so but may affect T-cell activation via APC derived cytokines such as IFN type I.

10/3,K/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10782537 PMID: 10903720

***CpG* -DNA-mediated transient lymphadenopathy is associated with a state of Th1 predisposition to antigen-driven responses.**

Lipford G B; Sparwasser T; Zimmermann S; Heeg K; Wagner H

Institute for Medical Microbiology, Immunology and Hygiene, Klinikum Rechts der Isar, Technical University of Munich, Munich, Germany. G.B.Lipford@lrz.tum.de

Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Aug 1 2000, 165 (3) p1228-35, ISSN 0022-1767 Journal Code: 2985117R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

***CpG* -DNA-mediated transient lymphadenopathy is associated with a state of Th1 predisposition to antigen-driven responses.**

Infections can influence concurrent and subsequent Th1 vs Th2 immune responses to Ags. Through pattern recognition of foreign unmethylated *CpG* dinucleotides, the vertebrate innate immune system can sense infectious danger and typically replies with a Th1-polarized adaptive immune response. We examined whether *CpG*-DNA exposure would influence subsequent responses to infection and soluble Ags. *CpG* -DNA injection led to local lymphadenopathy characterized by maintenance of cellular composition with some biasing toward elevated *dendritic* cell composition. Sustained local production of IL-12 and IFN-gamma from *dendritic* cells and T cells was shown. Prior injection by up to 2 wk with *CpG*-DNA protected BALB/c mice from Th2 driven lethal leishmaniasis. *CpG*-DNA injection by up to 5 wk before soluble Ag challenge resulted in the generation of Ag-specific CTL, Th1 recall responses to Ag, and Th1-polarized Ag-specific Abs. Thus, *CpG* -DNA instigated a local predisposition for intense CTL responses and Th1-polarized immune responses to subsequent infections or Ag challenge. The induction by the innate...

Descriptors: Antigens--immunology--IM; **CpG* Islands--immunology--IM; *DNA--immunology--IM; *Lymphatic Diseases--immunology--IM; *Oligonucleotides--immunology--IM; *Th1 Cells--immunology--IM...; Transfer; Animals; Antigens--administration and dosage--AD; Antigens, CD11--biosynthesis--BI; Cytotoxicity, Immunologic; DNA--administration and dosage--AD; Immunity, Cellular; Immunity, Natural; Immunization; Injections, Subcutaneous; *Interferon* Type II--biosynthesis--BI; Interleukin-12--biosynthesis--BI; Kinetics; Leishmania major--immunology--IM; Leishmaniasis, Cutaneous

--immunology--IM; Leishmaniasis, Cutaneous--prevention and control--PC; Lymph Nodes...
Chemical Name: Antigens; Antigens, CD11; Oligonucleotides; Interleukin-12 ; *Interferon* Type II; Ovalbumin; DNA

10/3,K/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10620196 PMID: 10725803
Stimulatory and inhibitory maturation of human macrophage-derived *dendritic* cells.
Chakraborty A; Li L; Chakraborty N G; Mukherji B
Department of Medicine, University of Connecticut School of Medicine, Farmington, Conn., USA.
Pathobiology - journal of immunopathology, molecular and cellular biology (SWITZERLAND) 1999, 67 (5-6) p282-6, ISSN 1015-2008 Journal Code: 9007504
Contract/Grant No.: CA 61398; CA; NCI; CA 83130; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Stimulatory and inhibitory maturation of human macrophage-derived *dendritic* cells.
Circulating human macrophages are often used to generate *dendritic* cells (DCs) by culturing them in granulocyte macrophage-colony stimulating factor (GM-CSF) and interleukin-4 (IL-4). As DCs are superb antigen-presenting cells...
... peripheral macrophage-derived myeloid DCs can be stimulatory, in vitro cultures of myeloid DCs in GM-CSF and IL-4 followed by further maturation in *interferon*-gamma plus bacterial superantigens (as DC maturing agents) can give rise to DCs that are functionally inhibitory. The stimulatory DCs express higher amounts of costimulatory...

... interestingly, neutralization of the endogenously derived IL-10 with anti-IL-10 antibody with DC cultures as well as exposure of the inhibitory DCs to *CpG* oligonucleotides or to in vitro activated autologous CD4+ T helper cells repolarize them into stimulatory phenotype. Accordingly, these observations have important implications in translational research...
Descriptors: *Dendritic* Cells--immunology--IM; *Immune Tolerance --immunology--IM; *Immunity, Cellular--immunology--IM; *Macrophages --immunology--IM; Antigen Presentation--drug effects--DE; Cell Differentiation; Cells, Cultured; Granulocyte-Macrophage Colony-Stimulating Factor--pharmacology--PD; *Interferon* Type II--pharmacology--PD; Interleukin-10--metabolism--ME; Interleukin-12--metabolism--ME; Interleukin -4--pharmacology--PD; Lymphocyte Culture Test, Mixed; Phytohemagglutinins --pharmacology--PD; Staphylococcus aureus...
Chemical Name: Phytohemagglutinins; Superantigens; Interleukin-10; Interleukin-12; Interleukin-4; *Interferon* Type II; Granulocyte-Macrophage Colony-Stimulating Factor

10/3,K/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10549963 PMID: 10651934
Immunostimulatory bacterial DNA sequences activate *dendritic* cells and promote priming and differentiation of CD8+ T cells.
Tascon R E; Ragno S; Lowrie D B; Colston M J
Mycobacterial Division, National Institute for Medical Research, London, UK.
Immunology (ENGLAND) Jan 2000, 99 (1) p1-7, ISSN 0019-2805 Journal Code: 0374672

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Immunostimulatory bacterial DNA sequences activate *dendritic* cells and promote priming and differentiation of CD8+ T cells.

CD8+ T lymphocytes producing high levels of *interferon* -gamma (IFN-gamma) and expressing antigen specific cytotoxic activity are effectively induced after plasmid DNA vaccination and mediate protection against several intracellular micro-organisms. Recent evidence suggests that the priming of CD8+ T-cell responses following DNA injection involves antigen presentation mediated by *dendritic* cells. Here, we show that bacterial DNA and synthetic oligonucleotides containing dinucleotide (*CpG*) motifs activate cytokine expression in *dendritic* cells and modulate in vivo CD8+ T-cell priming and differentiation.

Descriptors: CD8-Positive T-Lymphocytes--immunology--IM; **CpG* Islands; *DNA, Bacterial--immunology--IM; **Dendritic* Cells--immunology--IM; * *Interferon* Type II--secretion--SE; *Lymphocyte Activation

Chemical Name: DNA, Bacterial; Receptors, Antigen, T-Cell; Vaccines, Synthetic; *Interferon* Type II

10/3,K/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10475241 PMID: 10570325

Anti-double-stranded DNA antibodies and immunostimulatory plasmid DNA in combination mimic the endogenous IFN-alpha inducer in systemic lupus erythematosus.

Vallin H; Perers A; Alm G V; Ronnblom L

Section of Immunology, Department of Veterinary Microbiology, Swedish University of Agricultural Sciences, Uppsala, Sweden.

Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Dec 1 1999, 163 (11) p6306-13, ISSN 0022-1767 Journal Code: 2985117R

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... human monoclonal anti-ss/dsDNA Ab had the same effect. This IFN-alpha-inducing activity of the plasmid was abolished by methylation, suggesting that unmethylated *CpG* DNA motifs were important. Like IIF in SLE serum, the combination of SLE-IgG and pcDNA3 appeared to stimulate IFN-alpha production in natural IFN-alpha-producing cells, a unique cell population resembling immature *dendritic* cells. The IFN-alpha production was greatly enhanced by IFN-alpha2b and IFN-beta, and for SLE-IIF it was also enhanced by GM-CSF...

Descriptors: Autoantibodies--immunology--IM; *DNA--immunology--IM; * *Interferon*-alpha--secretion--SE; *Lupus Erythematosus, Systemic --immunology--IM; *Plasmids--immunology--IM; Antigen-Antibody Complex; Cytokines--pharmacology--PD; *Dendritic* Cells--immunology--IM; Gene Expression Regulation; Immunoglobulin G--immunology--IM; Leukocytes, Mononuclear--immunology--IM

Chemical Name: Antigen-Antibody Complex; Autoantibodies; Cytokines; Immunoglobulin G; *Interferon*-alpha; Plasmids; DNA

?ds

Set	Items	Description
S1	1	(CPG OR CG) (S) (POLYG OR POLY-G OR POLY(G))
S2	6	(ODN (W) 1585)
S3	0	S2 AND (PDC2 OR DENDRITIC)
S4	3	RD S2 (unique items)
S5	277	(DENDRITIC OR PDC2S OR IPCS) AND (CPG OR (ODN (W) 1585))
S6	0	S5 AND (POLY(G))
S7	77	S5 NOT PY>2000

```
S8          48   RD (unique items)
S9           7   S8 AND (INTERFERON)
S10          7   RD (unique items)
?s s8 and ((interferon (w) alpha) or (type (w) I (w) interferon))
              48  S8
          144289  INTERFERON
          596343  ALPHA
           26889  INTERFERON(W)ALPHA
          959757  TYPE
         1250621  I
          144289  INTERFERON
            2339  TYPE(W)I(W)INTERFERON
     S11       1  S8 AND ((INTERFERON (W) ALPHA) OR (TYPE (W) I (W)
                  INTERFERON))
?t s11/3,k/all

 11/3,K/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

10475241   PMID: 10570325
  Anti-double-stranded DNA antibodies and immunostimulatory plasmid DNA in
combination mimic the endogenous IFN-alpha inducer in systemic lupus
erythematosus.
  Vallin H; Perers A; Alm G V; Ronnblom L
  Section of Immunology, Department of Veterinary Microbiology, Swedish
University of Agricultural Sciences, Uppsala, Sweden.
  Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES)  Dec 1
1999, 163 (11) p6306-13, ISSN 0022-1767  Journal Code: 2985117R
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed

  ... human monoclonal anti-ss/dsDNA Ab had the same effect. This
IFN-alpha-inducing activity of the plasmid was abolished by methylation,
suggesting that unmethylated *CpG* DNA motifs were important. Like IIF in
SLE serum, the combination of SLE-IgG and pcDNA3 appeared to stimulate
IFN-alpha production in natural IFN-alpha-producing cells, a unique cell
population resembling immature *dendritic* cells. The IFN-alpha production
was greatly enhanced by IFN-alpha2b and IFN-beta, and for SLE-IIF it was
also enhanced by GM-CSF...
  Descriptors: Autoantibodies--immunology--IM; *DNA--immunology--IM; *
*Interferon*-*alpha*--secretion--SE; *Lupus Erythematosus, Systemic
--immunology--IM; *Plasmids--immunology--IM; Antigen-Antibody Complex;
Cytokines--pharmacology--PD; *Dendritic* Cells--immunology--IM; Gene
Expression Regulation; Immunoglobulin G--immunology--IM; Leukocytes,
Mononuclear--immunology--IM
  Chemical Name: Antigen-Antibody Complex; Autoantibodies; Cytokines;
Immunoglobulin G; *Interferon*-*alpha*; Plasmids; DNA
?ds

Set     Items   Description
S1          1   (CPG OR CG) (S) (POLYG OR POLY-G OR POLY(G))
S2          6   (ODN (W) 1585)
S3          0   S2 AND (PDC2 OR DENDRITIC)
S4          3   RD S2 (unique items)
S5        277   (DENDRITIC OR PDC2S OR IPCS) AND (CPG OR (ODN (W) 1585))
S6          0   S5 AND (POLY(G))
S7         77   S5 NOT PY>2000
S8         48   RD (unique items)
S9          7   S8 AND (INTERFERON)
S10         7   RD (unique items)
S11         1   S8 AND ((INTERFERON (W) ALPHA) OR (TYPE (W) I (W) INTERFER-
                ON))
?s s7 and (IL-12)
             77  S7
```

```
              2  IL-12
     S12      0  S7 AND (IL-12)
?s s7 and (interleukin-12 or (interleukin (w) 12))
             77  S7
           9963  INTERLEUKIN-12
         223635  INTERLEUKIN
         859739  12
          10836  INTERLEUKIN(W)12
     S13     32  S7 AND (INTERLEUKIN-12 OR (INTERLEUKIN (W) 12))
?t s13/3,k/all
```

13/3,K/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)
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14429574 PMID: 10427997

Oligodeoxynucleotides containing *CpG* motifs induce IL-12, IL-18 and IFN-gamma production in cells from allergic individuals and inhibit IgE synthesis in vitro.

Bohle B; Jahn-Schmid B; Maurer D; Kraft D; Ebner C
Department of General and Experimental Pathology, University of Vienna, Austria.

European journal of immunology (GERMANY) Jul 1999, 29 (7) p2344-53, ISSN 0014-2980 Journal Code: 1273201
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Oligodeoxynucleotides containing *CpG* motifs induce IL-12, IL-18 and IFN-gamma production in cells from allergic individuals and inhibit IgE synthesis in vitro.

The effects of phosphorothioate oligonucleotides containing *CpG* motifs (*CpG* -ODN) on cultured cells from allergic patients and non-atopic individuals were investigated. In peripheral blood mononuclear cells (PBMC) *CpG* -ODN led to a significant increase of IFN-gamma. By intracellular cytokine staining, IFN-gamma production could be attributed to NK cells and inhibition experiments indicated an IL-12-dependent mechanism. Moreover, *CpG* -ODN increased mRNA expression of IL-12 and IL-18 in PBMC. In this respect, no significant difference between allergic and non-atopic individuals was observed. Monocyte-derived *dendritic* cells were identified as one IL-12- and IL-18-producing source. In addition, stimulation of PBMC derived from atopic patients with *CpG*-ODN led to a considerable increase of polyclonal IgG and IgM synthesis. In contrast, the production of total IgE was suppressed. *CpG*-ODN induced a significant rise of IgG and IgM specific for allergens to which the patients were sensitized, whereas allergen-specific IgE levels remained unchanged. Our data suggest that *CpG* -ODN display a strong influence on the ongoing immune response and might represent potential adjuvants for specific immunotherapy of type I allergy.

Descriptors: Hay Fever--immunology--IM; *Immunoglobulin E--biosynthesis --BI; *Interferon Type II--biosynthesis--BI; **Interleukin*-*12* --biosynthesis--BI; *Interleukin-18--biosynthesis--BI; *Oligodeoxyribonucle otides--genetics--GE; *Oligodeoxyribonucleotides--pharmacology--PD; Base Sequence; *CpG* Islands; Hay Fever--genetics--GE; Immunoglobulin G --biosynthesis--BI; Immunoglobulin M--biosynthesis--BI; *Interleukin*-*12* --genetics--GE; Interleukin-18--genetics--GE; Killer Cells, Natural --immunology--IM; RNA, Messenger--genetics--GE; RNA, Messenger--metabolism --ME; Thionucleotides--genetics--GE; Thionucleotides--pharmacology--PD
Chemical Name: Immunoglobulin G; Immunoglobulin M; Interleukin-18; Oligodeoxyribonucleotides; RNA, Messenger; Thionucleotides; *Interleukin*-*12*; Immunoglobulin E; Interferon Type II

13/3,K/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

14321310 PMID: 10224474

Bacterial DNA and *CpG* -containing oligodeoxynucleotides activate cutaneous *dendritic* cells and induce IL-12 production: implications for the augmentation of Th1 responses.

Jakob T; Walker P S; Krieg A M; von Stebut E; Udey M C; Vogel J C

Dermatology Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA. thilo.jakob@gsf.de

International archives of allergy and immunology (SWITZERLAND) Feb-Apr 1999, 118 (2-4) p457-61, ISSN 1018-2438 Journal Code: 9211652

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Bacterial DNA and *CpG* -containing oligodeoxynucleotides activate cutaneous *dendritic* cells and induce IL-12 production: implications for the augmentation of Th1 responses.

BACKGROUND: Unmethylated *CpG* sequences in bacterial DNA act as adjuvants selectively inducing Th1 predominant immune responses during genetic vaccination or when used in conjunction with protein Ag. The precise mechanism of this adjuvant effect is unknown. Because *dendritic* cells (DC) are thought to be crucially involved in T cell priming and Th1/Th2 education during vaccination via skin, we characterized the effects of bacterial DNA and *CpG*-containing oligodeoxynucleotides (*CpG* ODN) on cutaneous DC. METHODS AND RESULTS: Stimulation with *CpG* ODN 1826 (6 micrograms/ml) induced activation of immature Langerhans cell (LC)-like DC as determined by an increased expression of MHC class II and costimulatory molecules, loss of E-cadherin-mediated adhesion and increased ability to stimulate allogeneic T cells. Composition-matched control ODN 1911 lacking *CpG* sequences at equal concentrations was without effect. In comparison to LPS and ODN 1911, *CpG* ODN 1826 selectively stimulated DC to release large amounts of IL-12 (p40) and little IL-6 or TNF-alpha within 18 h and detectable...

... p70 within 72 h. Stimulation with Escherichia coli DNA, but not calf thymus DNA, similarly induced DC maturation and IL-12 p40 production. Injection of *CpG* ODN into murine dermis induced enhanced expression of MHC class II and CD86 by LC in the overlying epidermis and intracytoplasmic IL-12 p40 accumulation in a subpopulation of activated LC. CONCLUSION: Bacterial DNA and *CpG* ODN stimulate DC in vitro and in vivo and may preferentially elicit Th1-predominant immune responses because they can activate and mobilize DC, inducing them...

Descriptors: *CpG* Islands--immunology--IM; *DNA, Bacterial--immunology --IM; **Dendritic* Cells--immunology--IM; **Interleukin*-*12*--immunology --IM; *Th1 Cells--immunology--IM

Chemical Name: DNA, Bacterial; Oligonucleotides; *Interleukin*-*12*

13/3,K/3 (Item 3 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

14111803 PMID: 9808567

Immunostimulatory *CpG* oligodeoxynucleotides enhance the immune response to vaccine strategies involving granulocyte-macrophage colony-stimulating factor.

Liu H M; Newbrough S E; Bhatia S K; Dahle C E; Krieg A M; Weiner G J

University of Iowa Interdisciplinary Graduate Program in Immunology, University of Iowa Department of Internal Medicine, University of Iowa Cancer Center, USA.

Blood (UNITED STATES) Nov 15 1998, 92 (10) p3730-6, ISSN 0006-4971 Journal Code: 7603509

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Immunostimulatory *CpG* oligodeoxynucleotides enhance the immune response to vaccine strategies involving granulocyte-macrophage colony-stimulating factor.

Immunostimulatory oligodeoxynucleotides containing the *CpG* motif (*CpG* ODN) can activate various immune cell subsets and induce production of a number of cytokines. Prior studies have demonstrated that both *CpG* ODN and granulocyte-macrophage colony-stimulating factor (GM-CSF) can serve as potent vaccine adjuvants. We used the 38C13 murine lymphoma system to evaluate the immune response to a combination of these two adjuvants. Immunization using antigen, *CpG* ODN, and soluble GM-CSF enhanced production of antigen-specific antibody and shifted production towards the IgG2a isotype, suggesting an enhanced TH1 response. This effect was most pronounced after repeat immunizations with *CpG* ODN and antigen/GM-CSF fusion protein. A single immunization with *CpG* ODN and antigen/GM-CSF fusion protein 3 days before tumor inoculation prevented tumor growth. *CpG* ODN enhanced the production of *interleukin*-*12* by bone marrow-derived *dendritic* cells and increased expression of major histocompatibility complex class I and class II molecules, particularly when cells were pulsed with antigen/GM-CSF fusion protein. We conclude that the use of *CpG* ODN in combination with strategies involving GM-CSF enhances the immune response to antigen and shifts the response towards a TH1 response and that this...

Descriptors: Adjuvants, Immunologic--pharmacology--PD; *Antigen Presentation--drug effects--DE; *Cancer Vaccines--immunology--IM; **CpG* Islands; *Granulocyte-Macrophage Colony-Stimulating Factor--pharmacology --PD; *Lymphoma, B-Cell--prevention and control--PC; *Oligodeoxyribonucleot ides--pharmacology--PD; *Th1 Cells--drug effects--DE; *Vaccination; *Vaccines...

; Animals; Antibodies, Anti-Idiotypic--biosynthesis--BI; Antigens --immunology--IM; *Dendritic* Cells--metabolism--ME; Granulocyte-Macrophage Colony-Stimulating Factor--genetics--GE; H-2 Antigens--biosynthesis--BI; Hemocyanin--immunology--IM; Histocompatibility Antigens Class II --biosynthesis--BI; Immunoglobulin G--biosynthesis--BI; Immunoglobulin G --immunology--IM; Immunoglobulin Idiotypes--immunology--IM; Immunoglobulin M--immunology--IM; *Interleukin*-*12*--biosynthesis--BI; Lymphoma, B-Cell --immunology--IM; Lymphoma, B-Cell--pathology--PA; Mice; Mice, Inbred C3H; Neoplasm Transplantation; Th1 Cells--immunology--IM

...Chemical Name: Antibodies, Anti-Idiotypic; Antigens; Cancer Vaccines; H-2 Antigens; Histocompatibility Antigens Class II; Immunoglobulin G; Immunoglobulin Idiotypes; Immunoglobulin M; Oligodeoxyribonucleotides; Vaccines, Synthetic; keyhole-limpet hemocyanin; *Interleukin*-*12*; Granulocyte-Macrophage Colony-Stimulating Factor; Hemocyanin

13/3,K/4 (Item 4 from file: 155)

14102134 PMID: 9799232

***CpG*-DNA-specific activation of antigen-presenting cells requires stress kinase activity and is preceded by non-specific endocytosis and endosomal maturation.**

Hacker H; Mischak H; Miethke T; Liptay S; Schmid R; Sparwasser T; Heeg K; Lipford G B; Wagner H

Institute of Medical Microbiology, Immunology and Hygiene, Technische Universitat Munchen, Trogerstrasse 9, D-81675 Munich, Germany.

EMBO journal (ENGLAND) Nov 2 1998, 17 (21) p6230-40, ISSN 0261-4189 Journal Code: 8208664

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

***CpG*-DNA-specific activation of antigen-presenting cells requires stress kinase activity and is preceded by non-specific endocytosis and endosomal maturation.**

Unmethylated *CpG* motifs in bacterial DNA, plasmid DNA and synthetic oligodeoxynucleotides (*CpG* ODN) activate *dendritic* cells (DC) and macrophages in a CD40-CD40 ligand-independent fashion. To understand the molecular mechanisms involved we focused on the cellular uptake of *CpG* ODN, the need for endosomal maturation and the role of the stress kinase pathway. Here we demonstrate that *CpG*-DNA induces phosphorylation of Jun N-terminal kinase kinase 1 (JNKK1/SEK/MKK4) and subsequent activation of the stress kinases JNK1/2 and p38 in murine macrophages and *dendritic* cells. This leads to activation of the transcription factor activating protein-1 (AP-1) via phosphorylation of its constituents c-Jun and ATF2. Moreover, stress kinase activation is essential for *CpG*-DNA-induced cytokine release of tumor necrosis factor alpha (TNFalpha) and *interleukin*-*12* (IL-12), as inhibition of p38 results in severe impairment of this biological response. We further demonstrate that cellular uptake via endocytosis and subsequent endosomal maturation is essential for signalling, since competition by non-*CpG*-DNA or compounds blocking endosomal maturation such as chloroquine or bafilomycin A prevent all aspects of cellular activation. The data suggest that endosomal maturation is required for translation of intraendosomal *CpG* ODN sequences into signalling via the stress kinase pathway, where p38 kinase activation represents an essential step in *CpG*-ODN-triggered activation of antigen-presenting cells.

13/3,K/5 (Item 5 from file: 155)

14042578 PMID: 9743369

Activation of cutaneous *dendritic* cells by *CpG* -containing oligodeoxynucleotides: a role for *dendritic* cells in the augmentation of Th1 responses by immunostimulatory DNA.

Jakob T; Walker P S; Krieg A M; Udey M C; Vogel J C
Dermatology Branch, National Cancer Institute, Bethesda, MD 20892-1908, USA.

Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Sep 15 1998, 161 (6) p3042-9, ISSN 0022-1767 Journal Code: 2985117R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Activation of cutaneous *dendritic* cells by *CpG* -containing oligodeoxynucleotides: a role for *dendritic* cells in the augmentation of Th1 responses by immunostimulatory DNA.

Genetic vaccination depends at least in part on the adjuvant properties of plasmids, properties that have been ascribed to unmethylated *CpG* dinucleotides in bacterial DNA. Because *dendritic* cells (DC) participate in the T cell priming that occurs during genetic vaccination, we reasoned that *CpG*-containing DNA might activate DC. Thus, we assessed the effects of *CpG* oligodeoxynucleotides (*CpG* ODN) on Langerhans cell (LC)-like murine fetal skin-derived DC (FSDDC) in vitro and on LC in vivo. Treatment with *CpG* ODN as well as LPS induced FSDDC maturation, manifested by decreased E-cadherin-mediated adhesion, up-regulation of MHC class II and costimulator molecule expression, and acquisition of enhanced accessory cell activity. In contrast to LPS, *CpG* ODN stimulated FSDDC to produce large amounts of IL-12 but only small amounts of IL-6 and TNF-alpha. Injection of *CpG* ODN into murine dermis also led to enhanced expression of MHC class II and CD86 Ag by LC in overlying epidermis and intracytoplasmic IL-12 accumulation in a subpopulation of activated LC. We conclude that immunostimulatory *CpG* ODN stimulate DC in vitro and in vivo. Bacterial DNA-based vaccines may preferentially elicit Th1-predominant immune responses because they activate and mobilize DC...

Descriptors: Adjuvants, Immunologic--pharmacology--PD; *DNA--immunology --IM; **Dendritic* Cells--immunology--IM; *Dinucleoside Phosphates --immunology--IM; *Oligodeoxyribonucleotides--immunology--IM; *Skin --immunology--IM; *Th1 Cells--immunology--IM; Animals; Antigen-Presenting

Cells--immunology--IM; Cell Differentiation--drug effects--DE; Cell Differentiation--immunology--IM; Cells, Cultured; DNA--pharmacology--PD; *Dendritic* Cells--cytology--CY; *Dendritic* Cells--metabolism--ME; Dinucleoside Phosphates--pharmacology--PD; Epidermis--drug effects--DE; Epidermis--immunology--IM; *Interleukin*-*12*--biosynthesis--BI; Langerhans Cells--drug effects--DE; Langerhans Cells--immunology--IM; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Oligodeoxyribonucleotides--pharmacology--PD; Skin--cytology--CY...

Chemical Name: Adjuvants, Immunologic; Dinucleoside Phosphates; Oligodeoxyribonucleotides; *Interleukin*-*12*; cytidylyl-3'-5'-guanosine; DNA

13/3,K/6 (Item 6 from file: 155)

13944376 PMID: 9645386

Bacterial DNA and immunostimulatory *CpG* oligonucleotides trigger maturation and activation of murine *dendritic* cells.

Sparwasser T; Koch E S; Vabulas R M; Heeg K; Lipford G B; Ellwart J W; Wagner H

Institute of Medical Microbiology, Immunology and Hygiene, Technical University of Munich, Germany.

European journal of immunology (GERMANY) Jun 1998, 28 (6) p2045-54, ISSN 0014-2980 Journal Code: 1273201

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Bacterial DNA and immunostimulatory *CpG* oligonucleotides trigger maturation and activation of murine *dendritic* cells.

Bacterial DNA and immunostimulatory (i.s.) synthetic *CpG* -oligodeoxynucleotides (ODN) act as adjuvants for Th1 responses and cytotoxic T cell responses to proteinaceous antigens. *Dendritic* cells (DC) can be referred to as "nature's adjuvant" since they display the unique capacity to sensitize naive T cells. Here, we demonstrate that bacterial DNA or i.s. *CpG*-ODN cause simultaneous maturation of immature DC and activation of mature DC to produce cytokines. These events are associated with the acquisition of professional antigen...

... and FACS-fractionated MHC class IIlow (termed immature DC) or MHC class IIhigh populations (termed mature DC) were stimulated with bacterial DNA or i.s. *CpG*-ODN. Similar to lipopolysaccharide, i.s. *CpG* -ODN caused up-regulation of MHC class II, CD40 and CD86, but not CD80 on immature and mature DC. In parallel, both DC subsets were activated to produce large amounts of IL-12, IL-6 and TNF-alpha. *CpG*-ODN-activated DC displayed professional APC function in allogeneic mixed lymphocyte reaction and in staphylococcal enterotoxin B-driven naive T cell responses. We interpret these findings to mean that bacterial DNA and i.s. *CpG*-ODN cause maturation (first step) and activation (second step) of DC to bring about conversion of immature DC into professional APC.

Descriptors: *CpG* Islands--immunology--IM; *DNA, Bacterial--immunology--IM; **Dendritic* Cells--immunology--IM; *Oligodeoxyribonucleotides--immunology--IM...; Immunologic; Animals; Antigens, CD40--metabolism--ME; Bone Marrow Cells; Cells, Cultured; Enzyme Induction; HLA-B7 Antigen--metabolism--ME; Hematopoiesis; Histocompatibility Antigens Class II--metabolism--ME; *Interleukin*-*12*--biosynthesis--BI; Interleukin-6--biosynthesis--BI; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Mice, Knockout; T-Lymphocytes, Cytotoxic--metabolism--ME; Tumor Necrosis Factor--biosynthesis...

Chemical Name: Adjuvants, Immunologic; Antigens, CD40; DNA, Bacterial; HLA-B7 Antigen; Histocompatibility Antigens Class II; Interleukin-6; Oligodeoxyribonucleotides; Tumor Necrosis Factor; *Interleukin*-*12*; beta-Galactosidase

13/3,K/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10943823 PMID: 11086063

Enhanced *dendritic* cell maturation by TNF-alpha or cytidine-phosphate-guanosine DNA drives T cell activation in vitro and therapeutic anti-tumor immune responses in vivo.

Brunner C; Seiderer J; Schlamp A; Bidlingmaier M; Eigler A; Haimerl W; Lehr H A; Krieg A M; Hartmann G; Endres S

Divisions of. Clinical Pharmacology and Neuroendocrinology, Departments of Medicine and Radiation Therapy, Ludwig-Maximilians-University of Munich, Munich, Germany.

Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Dec 1 2000, 165 (11) p6278-86, ISSN 0022-1767 Journal Code: 2985117R

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Enhanced *dendritic* cell maturation by TNF-alpha or cytidine-phosphate-guanosine DNA drives T cell activation in vitro and therapeutic anti-tumor immune responses in vivo.

Dendritic cells (DC) manipulated ex vivo can induce tumor immunity in experimental murine tumor models. To improve DC-based tumor vaccination, we studied whether DC maturation...

... bone marrow-derived DC was induced by GM-CSF plus IL-4 alone or by further addition of TNF-alpha or a cytidine-phosphate-guanosine (*CpG*)-containing oligonucleotide (ODN-1826), which mimics the immunostimulatory effect of bacterial DNA. Flow cytometric analysis of costimulatory molecules and MHC class II showed that DC...

... induction of alloreactive T cell proliferation. In BALB/c mice, s.c. injection of colon carcinoma cells resulted in rapidly growing tumors. In this model, *CpG*-ODN-stimulated DC cocultured with irradiated tumor cells also induced prophylactic protection most effectively and were therapeutically effective when administered 3 days after tumor challenge. Thus, *CpG*-ODN-enhanced DC maturation may represent an efficient means to improve clinical tumor vaccination.

Descriptors: Adjuvants, Immunologic--pharmacology--PD; *Antineoplastic Agents--immunology--IM; **CpG* Islands--immunology--IM; **Dendritic* Cells --immunology--IM; *Lymphocyte Activation--immunology--IM; *Oligodeoxyribonu cleotides--immunology--IM; *T-Lymphocytes--immunology--IM; *Tumor Necrosis Factor--immunology--IM...; Cell Communication--immunology--IM; Cell Differentiation--immunology--IM; Cells, Cultured; Coculture; Colonic Neoplasms--immunology--IM; Colonic Neoplasms--pathology--PA; Colonic Neoplasms--prevention and control--PC; *Dendritic* Cells--cytology--CY; *Dendritic* Cells--metabolism--ME; *Dendritic* Cells--transplantation--TR; Growth Inhibitors--immunology--IM; Growth Inhibitors--therapeutic use--TU; Immunotherapy, Adoptive--methods--MT; *Interleukin*-*12*--biosynthesis--BI; Interleukin-4--pharmacology--PD; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Neoplasm Transplantation; Oligodeoxyribonucleotides--therapeutic use --TU; Tumor Cells, Cultured--immunology--IM...

Chemical Name: Adjuvants, Immunologic; Antineoplastic Agents; *CPG* -oligonucleotide; Growth Inhibitors; Oligodeoxyribonucleotides; Tumor Necrosis Factor; *Interleukin*-*12*; Interleukin-4

13/3,K/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10943819 PMID: 11086059

APC stimulated by *CpG* oligodeoxynucleotide enhance activation of MHC class I-restricted T cells.

Warren T L; Bhatia S K; Acosta A M; Dahle C E; Ratliff T L; Krieg A M; Weiner G J

The Holden Cancer Center and Departments of Internal Medicine and Urology, University of Iowa, Iowa City, IA 522421, USA.

Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Dec 1 2000, 165 (11) p6244-51, ISSN 0022-1767 Journal Code: 2985117R

Contract/Grant No.: RO1CA74542; CA; NCI; T32 HL07344; HL; NHLBI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

APC stimulated by *CpG* oligodeoxynucleotide enhance activation of MHC class I-restricted T cells.

Oligonucleotides containing unmethylated *CpG* motifs (cytosine-phosphoro thioate-guanine oligodeoxynucleotide (*CpG* ODN)) are potent immunostimulatory agents capable of enhancing the Ag-specific Th1 response when used as immune adjuvants. We evaluated the cellular mechanisms responsible for this effect. Development of a CTL response was enhanced when mice were immunized with peptide-pulsed *dendritic* cells (DCs) treated with *CpG* ODN. However, in vitro, *CpG* ODN had no direct effect on highly purified T cells. In vitro, *CpG* ODN treatment of peptide- or protein-pulsed DCs enhanced the ability of the DCs to activate class I-restricted T cells. The presence of helper T cells enhanced this effect, indicating that treatment with *CpG* ODN does not obviate the role of T cell help. The enhanced ability of *CpG* ODN-treated DCs to activate T cells was present but blunted when DCs derived from IL-12 knockout mice were used. Fixation of Ag-pulsed, *CpG* ODN-treated DCs limited their ability to activate T cells. In contrast, fixation had little effect on DC activation of T cells when DCs were not exposed to *CpG* ODN. This indicates that production of soluble factors by DCs stimulated with *CpG* ODN plays a particularly important role in their ability to activate class I-restricted T cells. We conclude that *CpG* ODN enhances the development of a cellular immune response by stimulating APCs such as DCs, to produce IL-12 and other soluble factors.

; Animals; Antigen-Presenting Cells--metabolism--ME; Cytokines --biosynthesis--BI; Cytokines--physiology--PH; Cytotoxicity, Immunologic --genetics--GE; Cytotoxicity, Immunologic--immunology--IM; *Dendritic* Cells--immunology--IM; *Dendritic* Cells--metabolism--ME; Egg Proteins --immunology--IM; Egg Proteins--pharmacology--PD; Epitopes, T-Lymphocyte --immunology--IM; *Interleukin*-*12*--deficiency--DF; *Interleukin*-*12* --genetics--GE; *Interleukin*-*12*--physiology--PH; Lymphocyte Activation --genetics--GE; Mice; Mice, Inbred C3H; Mice, Inbred C57BL; Mice, Knockout; Mice, Transgenic; Oligodeoxyribonucleotides--pharmacology--PD; Ovalbumin --immunology--IM; Ovalbumin--pharmacology...

Chemical Name: Adjuvants, Immunologic; *CPG*-oligonucleotide; Cytokines; Egg Proteins; Epitopes, T-Lymphocyte; Histocompatibility Antigens Class I; OVA-8; Oligodeoxyribonucleotides; *Interleukin*-*12*; Ovalbumin

13/3,K/9 (Item 9 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10924082 PMID: 11069063

Response of human monocyte-derived *dendritic* cells to immunostimulatory DNA.

Schattenberg D; Schott M; Reindl G; Krueger T; Tschoepe D; Feldkamp J; Scherbaum W A; Seissler J

German Diabetes Research Institute, University of Dusseldorf.

European journal of immunology (GERMANY) Oct 2000, 30 (10) p2824-31, ISSN 0014-2980 Journal Code: 1273201

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Response of human monocyte-derived *dendritic* cells to immunostimulatory DNA.

Activated *dendritic* cells (DC) are of key importance for the initiation of primary immune responses and represent promising tools for immunotherapies in humans. Since DNA containing *CpG* motifs have been described as potent immunostimulatory (IS) adjuvants for murine DC, we here studied maturation and stimulation of functional activity in human monocyte-derived...

Descriptors: Adjuvants, Immunologic; **CpG* Islands; *DNA, Bacterial --immunology--IM; **Dendritic* Cells--immunology--IM; *Oligodeoxyribonucleotides--immunology--IM; *T-Lymphocytes--immunology--IM; Antigens, CD --biosynthesis--BI; Cell Differentiation--drug effects--DE; Deoxyribonucleases--pharmacology--PD; HLA-D Antigens--biosynthesis--BI; Immunoglobulins --biosynthesis--BI; Immunotherapy, Adoptive; *Interleukin*-*12*--secretion --SE; Interleukin-6--secretion--SE; Lymphocyte Activation; Membrane Glycoproteins--biosynthesis--BI; Monocytes--cytology--CY; Monocytes--drug effects--DE; Plasmids--genetics--GE; Species Specificity; T...

Chemical Name: Adjuvants, Immunologic; Antigens, CD; B7-2 protein; CD83 antigen; DNA, Bacterial; HLA-D Antigens; Immunoglobulins; Interleukin-6; Membrane Glycoproteins; Oligodeoxyribonucleotides; Plasmids; Tumor Necrosis Factor; *Interleukin*-*12*; Deoxyribonucleases

13/3,K/10 (Item 10 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10818110 PMID: 10944809

Immunostimulatory DNA sequences help to eradicate intracellular pathogens.

Wagner H; Hacker H; Lipford G B

Institute of Medical Microbiology, Immunology and Hygiene, Technical University of Munich, Germany.

Springer seminars in immunopathology (GERMANY) 2000, 22 (1-2) p147-52, ISSN 0344-4325 Journal Code: 7910384

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

; Adjuvants, Immunologic--pharmacology--PD; Animals; CD8-Positive T-Lymphocytes--immunology--IM; *CpG* Islands--immunology--IM; DNA --pharmacology--PD; *Dendritic* Cells--drug effects--DE; *Dendritic* Cells --immunology--IM; Endocytosis--drug effects--DE; Francisella tularensis --immunology--IM; Infection--immunology--IM; *Interleukin*-*12*--secretion --SE; Intracellular Fluid--virology--VI; Lipopolysaccharides--immunology --IM; Lipopolysaccharides--pharmacology--PD; Listeria monocytogenes --immunology--IM; MAP Kinase Signaling System--drug effects--DE; Mice; NF ...

Chemical Name: Adjuvants, Immunologic; Lipopolysaccharides; MAP Kinase Signaling System; NF-kappa B; Oligodeoxyribonucleotides; *Interleukin*-*12* ; DNA

13/3,K/11 (Item 11 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10818100 PMID: 10944799

Activation of skin *dendritic* cells by immunostimulatory DNA.

Vogel J C; Udey M C

Dermatology Branch, National Cancer Institute, Bethesda, MD 20892, USA.

Springer seminars in immunopathology (GERMANY) 2000, 22 (1-2) p45-54 , ISSN 0344-4325 Journal Code: 7910384

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Activation of skin *dendritic* cells by immunostimulatory DNA.

Descriptors: Adjuvants, Immunologic; *Antigens, Protozoan--immunology--IM; *DNA, Protozoan--immunology--IM; **Dendritic* Cells--immunology--IM; *Leishmania major--immunology--IM; *Metalloendopeptidases--genetics--GE; Animals; Antigen Presentation--drug effects--DE; Antigen Presentation --immunology--IM; Antigens, Protozoan--genetics--GE; Consensus Sequence; *CpG* Islands--immunology--IM; DNA, Protozoan--pharmacology--PD; DNA, Recombinant--immunology--IM; DNA, Recombinant--pharmacology--PD; Epidermis --immunology--IM; *Interleukin*-*12*--biosynthesis--BI; Leishmaniasis, Cutaneous--immunology--IM; Leishmaniasis, Cutaneous --prevention and control--PC; Metalloendopeptidases--immunology--IM; Mice; Mice, Inbred C57BL; Models, Immunological; Oligodeoxyribonucleotides--immunology--IM; Oligodeoxyribonucleotides...

Chemical Name: Adjuvants, Immunologic; Antigens, Protozoan; DNA, Protozoan; DNA, Recombinant; Oligodeoxyribonucleotides; Plasmids; Protozoan Vaccines; *Interleukin*-*12*; Metalloendopeptidases; glycoprotein gp63, Leishmania

13/3,K/12 (Item 12 from file: 155)

10782537 PMID: 10903720

***CpG* -DNA-mediated transient lymphadenopathy is associated with a state of Th1 predisposition to antigen-driven responses.**

Lipford G B; Sparwasser T; Zimmermann S; Heeg K; Wagner H

Institute for Medical Microbiology, Immunology and Hygiene, Klinikum Rechts der Isar, Technical University of Munich, Munich, Germany. G.B.Lipford@lrz.tum.de

Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Aug 1 2000, 165 (3) p1228-35, ISSN 0022-1767 Journal Code: 2985117R

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

***CpG* -DNA-mediated transient lymphadenopathy is associated with a state of Th1 predisposition to antigen-driven responses.**

Infections can influence concurrent and subsequent Th1 vs Th2 immune responses to Ags. Through pattern recognition of foreign unmethylated *CpG* dinucleotides, the vertebrate innate immune system can sense infectious danger and typically replies with a Th1-polarized adaptive immune response. We examined whether *CpG*-DNA exposure would influence subsequent responses to infection and soluble Ags. *CpG* -DNA injection led to local lymphadenopathy characterized by maintenance of cellular composition with some biasing toward elevated *dendritic* cell composition. Sustained local production of IL-12 and IFN-gamma from *dendritic* cells and T cells was shown. Prior injection by up to 2 wk with *CpG*-DNA protected BALB/c mice from Th2 driven lethal leishmaniasis. *CpG*-DNA injection by up to 5 wk before soluble Ag challenge resulted in the generation of Ag-specific CTL, Th1 recall responses to Ag, and Th1-polarized Ag-specific Abs. Thus, *CpG* -DNA instigated a local predisposition for intense CTL responses and Th1-polarized immune responses to subsequent infections or Ag challenge. The induction by the innate...

Descriptors: Antigens--immunology--IM; **CpG* Islands--immunology--IM; *DNA--immunology--IM; *Lymphatic Diseases--immunology--IM; *Oligonucleotides--immunology--IM; *Th1 Cells--immunology--IM...; dosage--AD; Antigens, CD11--biosynthesis--BI; Cytotoxicity, Immunologic; DNA--administration and dosage--AD; Immunity, Cellular; Immunity, Natural; Immunization; Injections, Subcutaneous; Interferon Type II--biosynthesis--BI; *Interleukin*-*12*--biosynthesis--BI; Kinetics; Leishmania major --immunology--IM; Leishmaniasis, Cutaneous--immunology--IM; Leishmaniasis, Cutaneous--prevention and control--PC; Lymph Nodes--immunology--IM; Lymph Nodes--metabolism--ME...

Chemical Name: Antigens; Antigens, CD11; Oligonucleotides; *Interleukin*-*12*; Interferon Type II; Ovalbumin; DNA

13/3,K/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10620196 PMID: 10725803
Stimulatory and inhibitory maturation of human macrophage-derived *dendritic* cells.
Chakraborty A; Li L; Chakraborty N G; Mukherji B
Department of Medicine, University of Connecticut School of Medicine, Farmington, Conn., USA.
Pathobiology - journal of immunopathology, molecular and cellular biology (SWITZERLAND) 1999, 67 (5-6) p282-6, ISSN 1015-2008 Journal Code: 9007504
Contract/Grant No.: CA 61398; CA; NCI; CA 83130; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Stimulatory and inhibitory maturation of human macrophage-derived *dendritic* cells.
Circulating human macrophages are often used to generate *dendritic* cells (DCs) by culturing them in granulocyte macrophage-colony stimulating factor (GM-CSF) and interleukin-4 (IL-4). As DCs are superb antigen-presenting cells...
... interestingly, neutralization of the endogenously derived IL-10 with anti-IL-10 antibody with DC cultures as well as exposure of the inhibitory DCs to *CpG* oligonucleotides or to in vitro activated autologous CD4+ T helper cells repolarize them into stimulatory phenotype. Accordingly, these observations have important implications in translational research...
Descriptors: *Dendritic* Cells--immunology--IM; *Immune Tolerance --immunology--IM; *Immunity, Cellular--immunology--IM; *Macrophages --immunology--IM; Antigen Presentation--drug effects--DE; Cell Differentiation; Cells, Cultured; Granulocyte-Macrophage Colony-Stimulating Factor--pharmacology--PD; Interferon Type II--pharmacology--PD; Interleukin-10--metabolism--ME; *Interleukin*-*12*--metabolism--ME; Interleukin-4--pharmacology--PD; Lymphocyte Culture Test, Mixed; Phytohemagglutinins--pharmacology--PD; Staphylococcus aureus--immunology --IM; Superantigens--pharmacology--PD
Chemical Name: Phytohemagglutinins; Superantigens; Interleukin-10; *Interleukin*-*12*; Interleukin-4; Interferon Type II; Granulocyte-Macrophage Colony-Stimulating Factor

13/3,K/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10606906 PMID: 10712665
The effects of DNA containing *CpG* motif on *dendritic* cells.
Behboudi S; Chao D; Klenerman P; Austyn J
Nuffield Department of Surgery, University of Oxford, John Radcliffe Hospital, Oxford, UK.
Immunology (ENGLAND) Mar 2000, 99 (3) p361-6, ISSN 0019-2805 Journal Code: 0374672
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The effects of DNA containing *CpG* motif on *dendritic* cells.
Dendritic cells (DC) are specialized antigen-presenting cells. DC can acquire and process antigens in the periphery before maturing and migrating

to secondary lymphoid tissues where they present the antigens and deliver co-stimulatory signals to T cells. We describe an immunostimulatory oligonucleotide containing a *CpG* motif that stimulated murine DC to up-regulate co-stimulatory molecules, induce T-cell proliferative responses and secrete *interleukin*-*12* in vitro. Administration of this oligonucleotide, but not of a control oligonucleotide lacking this motif, to mice led to the disappearance of DC from the marginal zone and T-cell areas of spleen, but not from heart or kidney. The same *CpG* did not cause maturation of monocyte-derived human DC in vitro, but lipopolysaccharide-treated monocyte-derived DC showed enhanced functional activity and up-regulated co...

Descriptors: *CpG* Islands; **Dendritic* Cells--immunology--IM; **Interleukin*-*12*--biosynthesis--BI; *Lectins, C-Type

...Chemical Name: CD; Antigens, CD40; B7-2 protein; DEC-205 receptor; Histocompatibility Antigens Class II; Integrin alphaXbeta2; Lectins, C-Type ; Lipopolysaccharides; Membrane Glycoproteins; Oligonucleotides; Receptors, Cell Surface; *Interleukin*-*12*

13/3,K/15 (Item 15 from file: 155)

10503141 PMID: 10601019

Cell type-specific activation of mitogen-activated protein kinases by *CpG*-DNA controls *interleukin*-*12* release from antigen-presenting cells.

Hacker H; Mischak H; Hacker G; Eser S; Prenzel N; Ullrich A; Wagner H

Institute of Medical Microbiology, Technische Universitat Munchen, Trogerstrasse 9, D-81675 Munich.

EMBO journal (ENGLAND) Dec 15 1999, 18 (24) p6973-82, ISSN 0261-4189 Journal Code: 8208664

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Cell type-specific activation of mitogen-activated protein kinases by *CpG*-DNA controls *interleukin*-*12* release from antigen-presenting cells.

Activation of antigen-presenting cells (APCs) by invariant constituents of pathogens such as lipopolysaccharide (LPS) or bacterial DNA (*CpG*-DNA) initiates immune responses. We have analyzed the mitogen-activated protein kinase (MAPK) pathways triggered by *CpG*-DNA and their significance for cytokine production in two subsets of APCs, i.e. macrophages and *dendritic* cells (DCs). We found that *CpG*-DNA induced extracellular signal-regulated kinase (ERK) activity in macrophages in a classic MEK-dependent way. This pathway up-regulated tumor necrosis factor production but down-regulated interleukin (IL)-12 production. However, in DCs, which produce large amounts of IL-12, *CpG*-DNA and LPS failed to induce ERK activity. Consistent with a specific negative regulatory role for ERK in macrophages, chemical activation of this pathway in DCs suppressed *CpG*-DNA-induced IL-12 production. Overall, these results imply that differential activation of MAP kinase pathways is a basic mechanism by which distinct subsets of...

Descriptors: Antigen-Presenting Cells--physiology--PH; **Dendritic* Cells --physiology--PH; **Interleukin*-*12*--biosynthesis--BI; **Interleukin*-*12*--genetics--GE; *Macrophages--physiology--PH; *Mitogen-Activated Protein Kinases--metabolism--ME; *Oligodeoxyribonucleotides--pharmacology --PD...; Antigen-Presenting Cells--drug effects--DE; Antigen-Presenting Cells--immunology--IM; Bone Marrow Cells--cytology--CY; Bone Marrow Cells --immunology--IM; Cell Line; Cells, Cultured; *Dendritic* Cells--drug effects--DE; *Dendritic* Cells--immunology--IM; Dinucleoside Phosphates; Gene Expression Regulation--immunology--IM; Lipopolysaccharides --pharmacology--PD; Luciferase--genetics--GE; Macrophages--drug effects--DE ; Macrophages--immunology--IM; Mice; Mice...

Chemical Name: Dinucleoside Phosphates; Lipopolysaccharides;

Oligodeoxyribonucleotides; Recombinant Proteins; Thionucleotides; Tumor Necrosis Factor; *Interleukin*-*12*; cytidylyl-3'-5'-guanosine; Luciferase; Mitogen-Activated Protein Kinases

13/3,K/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10475197 PMID: 10570281

Phosphorothioate oligodeoxynucleotides promote the in vitro development of human allergen-specific CD4+ T cells into Th1 effectors.

Parronchi P; Brugnolo F; Annunziato F; Manuelli C; Sampognaro S; Mavilia C; Romagnani S; Maggi E

Department of Internal Medicine, Immunoallergology and Respiratory Disease Unit, University of Florence, Florence, Italy.

Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Dec 1 1999, 163 (11) p5946-53, ISSN 0022-1767 Journal Code: 2985117R

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... the switch of murine immune responses from a Th2 to a Th1 profile of cytokine production that has been related to the activity of unmethylated *CpG* motifs present in bacterial, but not mammalian, DNA. We report here that some synthetic phosphorothioate, but not phosphodiester, oligodeoxynucleotides (ODNs) were able to induce B...

... bulk culture, suggesting that the Th1-inducing activity of phosphorothioate ODNs was mediated by their ability to stimulate the production of these cytokines by monocytes, *dendritic*, and NK cells. Cytosine methylation abolished the Th1-inducing activity of ODNs; however, *CpG* dinucleotide-containing ODNs exhibited the Th1-shifting effect independently of the presence or the absence of *CpG* motifs (5'-pur-pur-*CpG*-pyr-pyr-3'). Moreover, the inversion of *CpG* to GpC resulted only in a partial reduction of this activity, suggesting that the motif responsible for the Th1-skewing effect in humans is at...

...; Lymphocytes--immunology--IM; CD4-Positive T-Lymphocytes--cytology --CY; Cell Differentiation; Cytosine--immunology--IM; GC Rich Sequence --immunology--IM; Glycoproteins--immunology--IM; Interferons--biosynthesis --BI; *Interleukin*-*12*--biosynthesis--BI; Lymphocyte Activation; Mites --immunology--IM; Species Specificity; Th1 Cells--cytology--CY

Chemical Name: Allergens; Antigens, Dermatophagoides; Glycoproteins; Oligodeoxyribonucleotides; Thionucleotides; *Interleukin*-*12*; Cytosine; Interferons

13/3,K/17 (Item 1 from file: 159)
DIALOG(R)File 159:Cancerlit

02676752 20518845 PMID: 11069063

Response of human monocyte-derived *dendritic* cells to immunostimulatory DNA.

Schattenberg D; Schott M; Reindl G; Krueger T; Tschoepe D; Feldkamp J; Scherbaum W A; Seissler J

German Diabetes Research Institute, University of Dusseldorf.

Eur J Immunol (GERMANY) Oct 2000, 30 (10) p2824-31, ISSN 0014-2980 Journal Code: 1273201

Document Type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Response of human monocyte-derived *dendritic* cells to immunostimulatory DNA.

Activated *dendritic* cells (DC) are of key importance for the initiation of primary immune responses and represent promising tools for immunotherapies in humans. Since DNA containing *CpG* motifs have been described as potent immunostimulatory (IS) adjuvants for murine DC, we here studied maturation and stimulation of functional activity in human monocyte-derived...

Major Descriptors: Adjuvants, Immunologic; **CpG* Islands; *DNA, Bacterial--immunology--IM; **Dendritic* Cells--immunology--IM; *Oligodeoxyribonucleotides--immunology--IM; *T-Lymphocytes--immunology--IM

Minor Descriptors: Antigens, CD--biosynthesis--BI; Cell Differentiation --drug effects--DE; Deoxyribonucleases--pharmacology--PD; HLA-D Antigens --biosynthesis--BI; Immunoglobulins--biosynthesis--BI; Immunotherapy, Adoptive; *Interleukin*-*12*--secretion--SE; Interleukin-6--secretion--SE; Lymphocyte Transformation; Membrane Glycoproteins--biosynthesis--BI; Monocytes--cytology--CY; Monocytes--drug effects--DE; Plasmids--genetics --GE; Species Specificity; T...

Chemical Name: Adjuvants, Immunologic; Antigens, CD; B7-2 protein; CD83 antigen; DNA, Bacterial; HLA-D Antigens; Immunoglobulins; Interleukin-6; Membrane Glycoproteins; Oligodeoxyribonucleotides; Plasmids; Tumor Necrosis Factor; *Interleukin*-*12*; Deoxyribonucleases

13/3,K/18 (Item 2 from file: 159)

02675178 20540083 PMID: 11086063

Enhanced *dendritic* cell maturation by TNF-alpha or cytidine-phosphate-guanosine DNA drives T cell activation in vitro and therapeutic anti-tumor immune responses in vivo.

Brunner C; Seiderer J; Schlamp A; Bidlingmaier M; Eigler A; Haimerl W; Lehr H A; Krieg A M; Hartmann G; Endres S

Divisions of. Clinical Pharmacology and Neuroendocrinology, Departments of Medicine and Radiation Therapy, Ludwig-Maximilians-University of Munich, Munich, Germany.

J Immunol (UNITED STATES) Dec 1 2000, 165 (11) p6278-86, ISSN 0022-1767 Journal Code: 2985117R

Document Type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Enhanced *dendritic* cell maturation by TNF-alpha or cytidine-phosphate-guanosine DNA drives T cell activation in vitro and therapeutic anti-tumor immune responses in vivo.

Dendritic cells (DC) manipulated ex vivo can induce tumor immunity in experimental murine tumor models. To improve DC-based tumor vaccination, we studied whether DC maturation...

... bone marrow-derived DC was induced by GM-CSF plus IL-4 alone or by further addition of TNF-alpha or a cytidine-phosphate-guanosine (*CpG*)-containing oligonucleotide (ODN-1826), which mimics the immunostimulatory effect of bacterial DNA. Flow cytometric analysis of costimulatory molecules and MHC class II showed that DC...

... induction of alloreactive T cell proliferation. In BALB/c mice, s.c. injection of colon carcinoma cells resulted in rapidly growing tumors. In this model, *CpG*-ODN-stimulated DC cocultured with irradiated tumor cells also induced prophylactic protection most effectively and were therapeutically effective when administered 3 days after tumor challenge. Thus, *CpG*-ODN-enhanced DC maturation may represent an efficient means to improve clinical tumor vaccination.

Major Descriptors: Adjuvants, Immunologic--pharmacology--PD; *Antineoplastic Agents--immunology--IM; **CpG* Islands--immunology--IM; **Dendritic* Cells--immunology--IM; *Lymphocyte Transformation--immunology --IM; *Oligodeoxyribonucleotides--immunology--IM; *T-Lymphocytes--immunology--IM; *Tumor Necrosis Factor--immunology--IM

...Minor Descriptors: Cell Communication--immunology--IM; Cell Differentiation--immunology--IM; Cells, Cultured; Coculture; Colonic Neoplasms--immunology--IM; Colonic Neoplasms--pathology--PA; Colonic Neoplasms--prevention and control--PC; *Dendritic* Cells--cytology--CY; *Dendritic* Cells--metabolism--ME; *Dendritic* Cells--transplantation--TR; Growth Inhibitors--immunology--IM; Growth Inhibitors--therapeutic use--TU; Immunotherapy, Adoptive--methods--MT; *Interleukin*-*12*--biosynthesis--BI; Interleukin-4--pharmacology--PD; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Neoplasm Transplantation; Oligodeoxyribonucleotides--therapeutic use --TU; Tumor Cells, Cultured--immunology--IM...

Chemical Name: Adjuvants, Immunologic; Antineoplastic Agents; *CPG* -oligonucleotide; Growth Inhibitors; Oligodeoxyribonucleotides; Tumor Necrosis Factor; *Interleukin*-*12*; Interleukin-4

13/3,K/19 (Item 3 from file: 159)

02675175 20540079 PMID: 11086059

APC stimulated by *CpG* oligodeoxynucleotide enhance activation of MHC class I-restricted T cells.

Warren T L; Bhatia S K; Acosta A M; Dahle C E; Ratliff T L; Krieg A M; Weiner G J

The Holden Cancer Center and Departments of Internal Medicine and Urology, University of Iowa, Iowa City, IA 522421, USA.

J Immunol (UNITED STATES) Dec 1 2000, 165 (11) p6244-51, ISSN 0022-1767 Journal Code: 2985117R

Contract/Grant No.: RO1CA74542; CA; NCI; T32 HL07344; HL; NHLBI

Document Type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

APC stimulated by *CpG* oligodeoxynucleotide enhance activation of MHC class I-restricted T cells.

Oligonucleotides containing unmethylated *CpG* motifs (cytosine-phosphoro thioate-guanine oligodeoxynucleotide (*CpG* ODN)) are potent immunostimulatory agents capable of enhancing the Ag-specific Th1 response when used as immune adjuvants. We evaluated the cellular mechanisms responsible for this effect. Development of a CTL response was enhanced when mice were immunized with peptide-pulsed *dendritic* cells (DCs) treated with *CpG* ODN. However, in vitro, *CpG* ODN had no direct effect on highly purified T cells. In vitro, *CpG* ODN treatment of peptide- or protein-pulsed DCs enhanced the ability of the DCs to activate class I-restricted T cells. The presence of helper T cells enhanced this effect, indicating that treatment with *CpG* ODN does not obviate the role of T cell help. The enhanced ability of *CpG* ODN-treated DCs to activate T cells was present but blunted when DCs derived from IL-12 knockout mice were used. Fixation of Ag-pulsed, *CpG* ODN-treated DCs limited their ability to activate T cells. In contrast, fixation had little effect on DC activation of T cells when DCs were not exposed to *CpG* ODN. This indicates that production of soluble factors by DCs stimulated with *CpG* ODN plays a particularly important role in their ability to activate class I-restricted T cells. We conclude that *CpG* ODN enhances the development of a cellular immune response by stimulating APCs such as DCs, to produce IL-12 and other soluble factors.

Minor Descriptors: Antigen-Presenting Cells--metabolism--ME; Cytokines --biosynthesis--BI; Cytokines--physiology--PH; Cytotoxicity, Immunologic --genetics--GE; Cytotoxicity, Immunologic--immunology--IM; *Dendritic* Cells--immunology--IM; *Dendritic* Cells--metabolism--ME; Egg Proteins --immunology--IM; Egg Proteins--pharmacology--PD; Epitopes, T-Lymphocyte --immunology--IM; *Interleukin*-*12*--deficiency--DF; *Interleukin*-*12* --genetics--GE; *Interleukin*-*12*--physiology--PH; Lymphocyte Transformat ion--genetics--GE; Mice; Mice, Inbred C3H; Mice, Inbred C57BL; Mice, Knockout; Mice, Transgenic; Oligodeoxyribonucleotides--pharmacology--PD; Ovalbumin--immunology--IM; Ovalbumin--pharmacology...

Chemical Name: Adjuvants, Immunologic; *CPG*-oligonucleotide; Cytokines; Egg Proteins; Epitopes, T-Lymphocyte; Histocompatibility Antigens Class I; OVA-8; Oligodeoxyribonucleotides; *Interleukin*-*12*; Ovalbumin

13/3,K/20 (Item 4 from file: 159)
DIALOG(R)File 159:Cancerlit

02654360 20401096 PMID: 10944799
Activation of skin *dendritic* cells by immunostimulatory DNA.
Vogel J C; Udey M C
Dermatology Branch, National Cancer Institute, Bethesda, MD 20892, USA.
Springer Semin Immunopathol (GERMANY) 2000, 22 (1-2) p45-54, ISSN 0172-6641 Journal Code: 7910384
Document Type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Activation of skin *dendritic* cells by immunostimulatory DNA.
Major Descriptors: Adjuvants, Immunologic; *Antigens, Protozoan --immunology--IM; *DNA, Protozoan--immunology--IM; **Dendritic* Cells --immunology--IM; *Leishmania major--immunology--IM; *Metalloendopeptidases --genetics--GE
Minor Descriptors: Antigen Presentation--drug effects--DE; Antigen Presentation--immunology--IM; Antigens, Protozoan--genetics--GE; Consensus Sequence; *CpG* Islands--immunology--IM; DNA, Protozoan--pharmacology--PD; DNA, Recombinant--immunology--IM; DNA, Recombinant--pharmacology--PD; Epidermis--immunology--IM; *Interleukin*-*12*--biosynthesis--BI; Leishmania sis, Cutaneous--immunology--IM; Leishmaniasis, Cutaneous--prevention and control--PC; Metalloendopeptidases--immunology--IM; Mice; Mice, Inbred C57BL; Models, Immunological; Oligodeoxyribonucleotides--immunology--IM; Oligodeoxyribonucleotides...
Chemical Name: Adjuvants, Immunologic; Antigens, Protozoan; DNA, Protozoan; DNA, Recombinant; Oligodeoxyribonucleotides; Plasmids; Protozoan Vaccines; *Interleukin*-*12*; Metalloendopeptidases; glycoprotein gp63, Leishmania

13/3,K/21 (Item 5 from file: 159)
DIALOG(R)File 159:Cancerlit

02654355 20401106 PMID: 10944809
Immunostimulatory DNA sequences help to eradicate intracellular pathogens.
Wagner H; Hacker H; Lipford G B
Institute of Medical Microbiology, Immunology and Hygiene, Technical University of Munich, Germany.
Springer Semin Immunopathol (GERMANY) 2000, 22 (1-2) p147-52, ISSN 0172-6641 Journal Code: 7910384
Document Type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Minor Descriptors: Adjuvants, Immunologic--pharmacology--PD; CD8-Positive T-Lymphocytes--immunology--IM; *CpG* Islands--immunology--IM; DNA --pharmacology--PD; *Dendritic* Cells--drug effects--DE; *Dendritic* Cells --immunology--IM; Endocytosis--drug effects--DE; Francisella tularensis --immunology--IM; Infection--immunology--IM; *Interleukin*-*12*--secretion --SE; Intracellular Fluid--virology--VI; Lipopolysaccharides--immunology --IM; Lipopolysaccharides--pharmacology--PD; Listeria monocytogenes --immunology--IM; MAP Kinase Signaling System--drug effects--DE; Mice; NF ...
Chemical Name: Adjuvants, Immunologic; Lipopolysaccharides; MAP Kinase

Signaling System; NF-kappa B; Oligodeoxyribonucleotides; *Interleukin*-*12* ; DNA

13/3,K/22 (Item 6 from file: 159)
DIALOG(R)File 159:Cancerlit
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02646238 20363803 PMID: 10903720
***CpG* -DNA-mediated transient lymphadenopathy is associated with a state of Th1 predisposition to antigen-driven responses.**
Lipford G B; Sparwasser T; Zimmermann S; Heeg K; Wagner H
Institute for Medical Microbiology, Immunology and Hygiene, Klinikum Rechts der Isar, Technical University of Munich, Munich, Germany. G.B.Lipford@lrz.tum.de
J Immunol (UNITED STATES) Aug 1 2000, 165 (3) p1228-35, ISSN 0022-1767 Journal Code: 2985117R
Document Type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

***CpG* -DNA-mediated transient lymphadenopathy is associated with a state of Th1 predisposition to antigen-driven responses.**
Infections can influence concurrent and subsequent Th1 vs Th2 immune responses to Ags. Through pattern recognition of foreign unmethylated *CpG* dinucleotides, the vertebrate innate immune system can sense infectious danger and typically replies with a Th1-polarized adaptive immune response. We examined whether *CpG*-DNA exposure would influence subsequent responses to infection and soluble Ags. *CpG* -DNA injection led to local lymphadenopathy characterized by maintenance of cellular composition with some biasing toward elevated *dendritic* cell composition. Sustained local production of IL-12 and IFN-gamma from *dendritic* cells and T cells was shown. Prior injection by up to 2 wk with *CpG*-DNA protected BALB/c mice from Th2 driven lethal leishmaniasis. *CpG*-DNA injection by up to 5 wk before soluble Ag challenge resulted in the generation of Ag-specific CTL, Th1 recall responses to Ag, and Th1-polarized Ag-specific Abs. Thus, *CpG* -DNA instigated a local predisposition for intense CTL responses and Th1-polarized immune responses to subsequent infections or Ag challenge. The induction by the innate...
Major Descriptors: Antigens--immunology--IM; **CpG* Islands--immunology --IM; *DNA--immunology--IM; *Lymphatic Diseases--immunology--IM; *Oligonucleotides--immunology--IM; *Th1 Cells--immunology--IM
...Minor Descriptors: dosage--AD; Antigens, CD11--biosynthesis--BI; Cytotoxicity, Immunologic; DNA--administration and dosage--AD; Immunity, Cellular; Immunity, Natural; Immunization; Injections, Subcutaneous; Interferon Type II--biosynthesis--BI; *Interleukin*-*12*--biosynthesis--BI; Kinetics; Leishmania major--immunology--IM; Leishmaniasis, Cutaneous --immunology--IM; Leishmaniasis, Cutaneous--prevention and control--PC; Lymph Nodes--immunology--IM; Lymph Nodes--metabolism--ME...
Chemical Name: Antigens; Antigens, CD11; Oligonucleotides; *Interleukin*-*12*; Interferon Type II; Ovalbumin; DNA

13/3,K/23 (Item 7 from file: 159)
DIALOG(R)File 159:Cancerlit
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02614841 20177722 PMID: 10712665
The effects of DNA containing *CpG* motif on *dendritic* cells.
Behboudi S; Chao D; Klenerman P; Austyn J
Nuffield Department of Surgery, University of Oxford, John Radcliffe Hospital, Oxford, UK.
Immunology (ENGLAND) Mar 2000, 99 (3) p361-6, ISSN 0019-2805 Journal Code: 0374672
Document Type: Journal Article
Languages: ENGLISH

Main Citation Owner: NLM
Record type: Completed

The effects of DNA containing *CpG* motif on *dendritic* cells.
Dendritic cells (DC) are specialized antigen-presenting cells. DC can acquire and process antigens in the periphery before maturing and migrating to secondary lymphoid tissues where they present the antigens and deliver co-stimulatory signals to T cells. We describe an immunostimulatory oligonucleotide containing a *CpG* motif that stimulated murine DC to up-regulate co-stimulatory molecules, induce T-cell proliferative responses and secrete *interleukin*-*12* in vitro. Administration of this oligonucleotide, but not of a control oligonucleotide lacking this motif, to mice led to the disappearance of DC from the marginal zone and T-cell areas of spleen, but not from heart or kidney. The same *CpG* did not cause maturation of monocyte-derived human DC in vitro, but lipopolysaccharide-treated monocyte-derived DC showed enhanced functional activity and up-regulated co...
Major Descriptors: *CpG* Islands; **Dendritic* Cells--immunology--IM; **Interleukin*-*12*--biosynthesis--BI
Chemical Name: Antigens, CD; Antigens, CD40; B7-2 protein; Complement 4-Binding Protein; DEC-205 receptor; Histocompatibility Antigens Class II; Lipopolysaccharides; Membrane Glycoproteins; Oligonucleotides; Receptors, Cell Surface; *Interleukin*-*12*

13/3,K/24 (Item 8 from file: 159)
DIALOG(R)File 159:Cancerlit

02595787 20191604 PMID: 10725803
Stimulatory and inhibitory maturation of human macrophage-derived *dendritic* cells.
Chakraborty A; Li L; Chakraborty N G; Mukherji B
Department of Medicine, University of Connecticut School of Medicine, Farmington, Conn., USA.
Pathobiology (SWITZERLAND) 1999, 67 (5-6) p282-6, ISSN 1015-2008 Journal Code: 9007504
Contract/Grant No.: CA 61398; CA; NCI; CA 83130; CA; NCI
Document Type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Stimulatory and inhibitory maturation of human macrophage-derived *dendritic* cells.
Circulating human macrophages are often used to generate *dendritic* cells (DCs) by culturing them in granulocyte macrophage-colony stimulating factor (GM-CSF) and interleukin-4 (IL-4). As DCs are superb antigen-presenting cells...
... interestingly, neutralization of the endogenously derived IL-10 with anti-IL-10 antibody with DC cultures as well as exposure of the inhibitory DCs to *CpG* oligonucleotides or to in vitro activated autologous CD4+ T helper cells repolarize them into stimulatory phenotype. Accordingly, these observations have important implications in translational research...
Major Descriptors: *Dendritic* Cells--immunology--IM; *Immune Tolerance --immunology--IM; *Immunity, Cellular--immunology--IM; *Macrophages --immunology--IM
Minor Descriptors: Antigen Presentation--drug effects--DE; Cell Differentiation; Cells, Cultured; Granulocyte-Macrophage Colony-Stimulating Factor--pharmacology--PD; Interferon Type II--pharmacology--PD; Interleukin-10--metabolism--ME; *Interleukin*-*12*--metabolism--ME; Interleukin-4--pharmacology--PD; Lymphocyte Culture Test, Mixed; Phytohemagglutinins--pharmacology--PD; Staphylococcus aureus--immunology --IM; Superantigens--pharmacology--PD
Chemical Name: Phytohemagglutinins; Superantigens; Interleukin-10; *Interleukin*-*12*; Interleukin-4; Interferon Type II; Granulocyte-Macrophage Colony-Stimulating Factor

13/3,K/25 (Item 9 from file: 159)
DIALOG(R)File 159:Cancerlit
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02587916 20069327 PMID: 10601019

Cell type-specific activation of mitogen-activated protein kinases by *CpG*-DNA controls *interleukin*-*12* release from antigen-presenting cells.

Hacker H; Mischak H; Hacker G; Eser S; Prenzel N; Ullrich A; Wagner H

Institute of Medical Microbiology, Technische Universitat Munchen, Trogerstrasse 9, D-81675 Munich.

EMBO J (ENGLAND) Dec 15 1999, 18 (24) p6973-82, ISSN 0261-4189 Journal Code: 8208664

Document Type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Cell type-specific activation of mitogen-activated protein kinases by *CpG*-DNA controls *interleukin*-*12* release from antigen-presenting cells.

Activation of antigen-presenting cells (APCs) by invariant constituents of pathogens such as lipopolysaccharide (LPS) or bacterial DNA (*CpG*-DNA) initiates immune responses. We have analyzed the mitogen-activated protein kinase (MAPK) pathways triggered by *CpG*-DNA and their significance for cytokine production in two subsets of APCs, i.e. macrophages and *dendritic* cells (DCs). We found that *CpG*-DNA induced extracellular signal-regulated kinase (ERK) activity in macrophages in a classic MEK-dependent way. This pathway up-regulated tumor necrosis factor production but down-regulated interleukin (IL)-12 production. However, in DCs, which produce large amounts of IL-12, *CpG*-DNA and LPS failed to induce ERK activity. Consistent with a specific negative regulatory role for ERK in macrophages, chemical activation of this pathway in DCs suppressed *CpG*-DNA-induced IL-12 production. Overall, these results imply that differential activation of MAP kinase pathways is a basic mechanism by which distinct subsets of...

Major Descriptors: Antigen-Presenting Cells--physiology--PH; **Dendritic* Cells--physiology--PH; **Interleukin*-*12*--biosynthesis--BI; **Interleukin*-*12*--genetics--GE; *Macrophages--physiology--PH; *Mitogen-Activated Protein Kinases--metabolism--ME; *Oligodeoxyribonucleotides--pharmacology--PD

Minor Descriptors: Antigen-Presenting Cells--drug effects--DE; Antigen-Presenting Cells--immunology--IM; Bone Marrow Cells--cytology--CY; Bone Marrow Cells--immunology--IM; Cell Line; Cells, Cultured; *Dendritic* Cells--drug effects--DE; *Dendritic* Cells--immunology--IM; Dinucleoside Phosphates; Gene Expression Regulation--immunology--IM; Lipopolysaccharides--pharmacology--PD; Luciferase--genetics--GE; Macrophages--drug effects--DE; Macrophages--immunology--IM; Mice; Mice...

Chemical Name: Dinucleoside Phosphates; Lipopolysaccharides; Oligodeoxyribonucleotides; Recombinant Proteins; Thionucleotides; Tumor Necrosis Factor; *Interleukin*-*12*; cytidylyl-3'-5'-guanosine; Luciferase; Mitogen-Activated Protein Kinases

13/3,K/26 (Item 10 from file: 159)
DIALOG(R)File 159:Cancerlit
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02580519 20040386 PMID: 10570281

Phosphorothioate oligodeoxynucleotides promote the in vitro development of human allergen-specific CD4+ T cells into Th1 effectors.

Parronchi P; Brugnolo F; Annunziato F; Manuelli C; Sampognaro S; Mavilia C; Romagnani S; Maggi E

Department of Internal Medicine, Immunoallergology and Respiratory Disease Unit, University of Florence, Florence, Italy.

J Immunol (UNITED STATES) Dec 1 1999, 163 (11) p5946-53, ISSN 0022-1767 Journal Code: 2985117R
Document Type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... the switch of murine immune responses from a Th2 to a Th1 profile of cytokine production that has been related to the activity of unmethylated *CpG* motifs present in bacterial, but not mammalian, DNA. We report here that some synthetic phosphorothioate, but not phosphodiester, oligodeoxynucleotides (ODNs) were able to induce B...

... bulk culture, suggesting that the Th1-inducing activity of phosphorothioate ODNs was mediated by their ability to stimulate the production of these cytokines by monocytes, *dendritic*, and NK cells. Cytosine methylation abolished the Th1-inducing activity of ODNs; however, *CpG* dinucleotide-containing ODNs exhibited the Th1-shifting effect independently of the presence or the absence of *CpG* motifs (5'-pur-pur-*CpG*-pyr-pyr-3'). Moreover, the inversion of *CpG* to GpC resulted only in a partial reduction of this activity, suggesting that the motif responsible for the Th1-skewing effect in humans is at...
...Minor Descriptors: Lymphocytes--immunology--IM; CD4-Positive T-Lymphocytes--cytology--CY; Cell Differentiation; Cytosine--immunology--IM ; GC Rich Sequence--immunology--IM; Glycoproteins--immunology--IM; Interferons--biosynthesis--BI; *Interleukin*-*12*--biosynthesis--BI; Lympho cyte Transformation; Mites--immunology--IM; Species Specificity; Th1 Cells --cytology--CY
Chemical Name: Allergens; Dermatophagoides allergens; Glycoproteins; Oligodeoxyribonucleotides; Thionucleotides; *Interleukin*-*12*; Cytosine; Interferons

13/3,K/27 (Item 11 from file: 159)
DIALOG(R)File 159:Cancerlit

02551716 99354951 PMID: 10427997
Oligodeoxynucleotides containing *CpG* motifs induce IL-12, IL-18 and IFN-gamma production in cells from allergic individuals and inhibit IgE synthesis in vitro.
Bohle B; Jahn-Schmid B; Maurer D; Kraft D; Ebner C
Department of General and Experimental Pathology, University of Vienna, Austria.
Eur J Immunol (GERMANY) Jul 1999, 29 (7) p2344-53, ISSN 0014-2980 Journal Code: 1273201
Document Type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Oligodeoxynucleotides containing *CpG* motifs induce IL-12, IL-18 and IFN-gamma production in cells from allergic individuals and inhibit IgE synthesis in vitro.
The effects of phosphorothioate oligonucleotides containing *CpG* motifs (*CpG* -ODN) on cultured cells from allergic patients and non-atopic individuals were investigated. In peripheral blood mononuclear cells (PBMC) *CpG* -ODN led to a significant increase of IFN-gamma. By intracellular cytokine staining, IFN-gamma production could be attributed to NK cells and inhibition experiments indicated an IL-12-dependent mechanism. Moreover, *CpG* -ODN increased mRNA expression of IL-12 and IL-18 in PBMC. In this respect, no significant difference between allergic and non-atopic individuals was observed. Monocyte-derived *dendritic* cells were identified as one IL-12- and IL-18-producing source. In addition, stimulation of PBMC derived from atopic patients with *CpG*-ODN led to a considerable increase of polyclonal IgG and IgM synthesis. In contrast, the production of total IgE was suppressed. *CpG*-ODN induced a significant

rise of IgG and IgM specific for allergens to which the patients were sensitized, whereas allergen-specific IgE levels remained unchanged. Our data suggest that *CpG* -ODN display a strong influence on the ongoing immune response and might represent potential adjuvants for specific immunotherapy of type I allergy.

Major Descriptors: Hay Fever--immunology--IM; *Immunoglobulin E --biosynthesis--BI; *Interferon Type II--biosynthesis--BI; **Interleukin*-*12*--biosynthesis--BI; *Interleukin-18--biosynthesis--BI; *Oligodeoxyribonucleotides--genetics--GE; *Oligodeoxyribonucleotides--pharmacology--PD

Minor Descriptors: Base Sequence; *CpG* Islands; Hay Fever--genetics--GE; Immunoglobulin G--biosynthesis--BI; Immunoglobulin M--biosynthesis--BI; *Interleukin*-*12*--genetics--GE; Interleukin-18--genetics--GE; Killer Cells, Natural--immunology--IM; RNA, Messenger--genetics--GE; RNA, Messenger--metabolism--ME; Thionucleotides--genetics--GE; Thionucleotides --pharmacology--PD

Chemical Name: Immunoglobulin G; Immunoglobulin M; Interleukin-18; Oligodeoxyribonucleotides; RNA, Messenger; Thionucleotides; *Interleukin*-*12*; Immunoglobulin E; Interferon Type II

13/3,K/28 (Item 12 from file: 159)

02530613 99242529 PMID: 10224474

Bacterial DNA and *CpG* -containing oligodeoxynucleotides activate cutaneous *dendritic* cells and induce IL-12 production: implications for the augmentation of Th1 responses.

Jakob T; Walker P S; Krieg A M; von Stebut E; Udey M C; Vogel J C

Dermatology Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA. thilo.jakob@gsf.de

Int Arch Allergy Immunol (SWITZERLAND) Feb-Apr 1999, 118 (2-4) p457-61, ISSN 1018-2438 Journal Code: 9211652

Document Type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Bacterial DNA and *CpG* -containing oligodeoxynucleotides activate cutaneous *dendritic* cells and induce IL-12 production: implications for the augmentation of Th1 responses.

BACKGROUND: Unmethylated *CpG* sequences in bacterial DNA act as adjuvants selectively inducing Th1 predominant immune responses during genetic vaccination or when used in conjunction with protein Ag. The precise mechanism of this adjuvant effect is unknown. Because *dendritic* cells (DC) are thought to be crucially involved in T cell priming and Th1/Th2 education during vaccination via skin, we characterized the effects of bacterial DNA and *CpG*-containing oligodeoxynucleotides (*CpG* ODN) on cutaneous DC. METHODS AND RESULTS: Stimulation with *CpG* ODN 1826 (6 micrograms/ml) induced activation of immature Langerhans cell (LC)-like DC as determined by an increased expression of MHC class II and costimulatory molecules, loss of E-cadherin-mediated adhesion and increased ability to stimulate allogeneic T cells. Composition-matched control ODN 1911 lacking *CpG* sequences at equal concentrations was without effect. In comparison to LPS and ODN 1911, *CpG* ODN 1826 selectively stimulated DC to release large amounts of IL-12 (p40) and little IL-6 or TNF-alpha within 18 h and detectable...

... p70 within 72 h. Stimulation with Escherichia coli DNA, but not calf thymus DNA, similarly induced DC maturation and IL-12 p40 production. Injection of *CpG* ODN into murine dermis induced enhanced expression of MHC class II and CD86 by LC in the overlying epidermis and intracytoplasmic IL-12 p40 accumulation in a subpopulation of activated LC. CONCLUSION: Bacterial DNA and *CpG* ODN stimulate DC in vitro and in vivo and may preferentially elicit Th1-predominant immune responses because they can activate and mobilize DC, inducing them...

Major Descriptors: *CpG* Islands--immunology--IM; *DNA, Bacterial

--immunology--IM; **Dendritic* Cells--immunology--IM; **Interleukin*-*12* --immunology--IM; *Th1 Cells--immunology--IM
Chemical Name: DNA, Bacterial; Oligonucleotides; *Interleukin*-*12*

13/3,K/29 (Item 13 from file: 159)
DIALOG(R)File 159:Cancerlit

02484337 99016044 PMID: 9799232

***CpG*-DNA-specific activation of antigen-presenting cells requires stress kinase activity and is preceded by non-specific endocytosis and endosomal maturation.**

Hacker H; Mischak H; Miethke T; Liptay S; Schmid R; Sparwasser T; Heeg K; Lipford G B; Wagner H
Institute of Medical Microbiology, Immunology and Hygiene, Technische Universitat Munchen, Trogerstrasse 9, D-81675 Munich, Germany.

EMBO J (ENGLAND) Nov 2 1998, 17 (21) p6230-40, ISSN 0261-4189
Journal Code: 8208664
Document Type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

***CpG*-DNA-specific activation of antigen-presenting cells requires stress kinase activity and is preceded by non-specific endocytosis and endosomal maturation.**

Unmethylated *CpG* motifs in bacterial DNA, plasmid DNA and synthetic oligodeoxynucleotides (*CpG* ODN) activate *dendritic* cells (DC) and macrophages in a CD40-CD40 ligand-independent fashion. To understand the molecular mechanisms involved we focused on the cellular uptake of *CpG* ODN, the need for endosomal maturation and the role of the stress kinase pathway. Here we demonstrate that *CpG*-DNA induces phosphorylation of Jun N-terminal kinase kinase 1 (JNKK1/SEK/MKK4) and subsequent activation of the stress kinases JNK1/2 and p38 in murine macrophages and *dendritic* cells. This leads to activation of the transcription factor activating protein-1 (AP-1) via phosphorylation of its constituents c-Jun and ATF2. Moreover, stress kinase activation is essential for *CpG*-DNA-induced cytokine release of tumor necrosis factor alpha (TNFalpha) and *interleukin*-*12* (IL-12), as inhibition of p38 results in severe impairment of this biological response. We further demonstrate that cellular uptake via endocytosis and subsequent endosomal maturation is essential for signalling, since competition by non-*CpG*-DNA or compounds blocking endosomal maturation such as chloroquine or bafilomycin A prevent all aspects of cellular activation. The data suggest that endosomal maturation is required for translation of intraendosomal *CpG* ODN sequences into signalling via the stress kinase pathway, where p38 kinase activation represents an essential step in *CpG*-ODN-triggered activation of antigen-presenting cells.

13/3,K/30 (Item 14 from file: 159)
DIALOG(R)File 159:Cancerlit

02481977 99025947 PMID: 9808567

Immunostimulatory *CpG* oligodeoxynucleotides enhance the immune response to vaccine strategies involving granulocyte-macrophage colony-stimulating factor.

Liu H M; Newbrough S E; Bhatia S K; Dahle C E; Krieg A M; Weiner G J
University of Iowa Interdisciplinary Graduate Program in Immunology, University of Iowa Department of Internal Medicine, University of Iowa Cancer Center, USA.

Blood (UNITED STATES) Nov 15 1998, 92 (10) p3730-6, ISSN 0006-4971
Journal Code: 7603509
Document Type: Journal Article
Languages: ENGLISH

Main Citation Owner: NLM
Record type: Completed

Immunostimulatory *CpG* oligodeoxynucleotides enhance the immune response to vaccine strategies involving granulocyte-macrophage colony-stimulating factor.

Immunostimulatory oligodeoxynucleotides containing the *CpG* motif (*CpG* ODN) can activate various immune cell subsets and induce production of a number of cytokines. Prior studies have demonstrated that both *CpG* ODN and granulocyte-macrophage colony-stimulating factor (GM-CSF) can serve as potent vaccine adjuvants. We used the 38C13 murine lymphoma system to evaluate the immune response to a combination of these two adjuvants. Immunization using antigen, *CpG* ODN, and soluble GM-CSF enhanced production of antigen-specific antibody and shifted production towards the IgG2a isotype, suggesting an enhanced TH1 response. This effect was most pronounced after repeat immunizations with *CpG* ODN and antigen/GM-CSF fusion protein. A single immunization with *CpG* ODN and antigen/GM-CSF fusion protein 3 days before tumor inoculation prevented tumor growth. *CpG* ODN enhanced the production of *interleukin*-*12* by bone marrow-derived *dendritic* cells and increased expression of major histocompatibility complex class I and class II molecules, particularly when cells were pulsed with antigen/GM-CSF fusion protein. We conclude that the use of *CpG* ODN in combination with strategies involving GM-CSF enhances the immune response to antigen and shifts the response towards a TH1 response and that this...

Major Descriptors: Adjuvants, Immunologic--pharmacology--PD; *Antigen Presentation--drug effects--DE; *Cancer Vaccines--immunology--IM; **CpG* Islands; *Granulocyte-Macrophage Colony-Stimulating Factor--pharmacology --PD; *Lymphoma, B-Cell--prevention and control--PC; *Oligodeoxyribonucleot ides--pharmacology--PD; *Th1 Cells--drug effects--DE; *Vaccination; *Vaccines...

Minor Descriptors: Antibodies, Anti-Idiotypic--biosynthesis--BI; Antigens --immunology--IM; *Dendritic* Cells--metabolism--ME; Granulocyte-Macrophage Colony-Stimulating Factor--genetics--GE; H-2 Antigens--biosynthesis--BI; Hemocyanin--immunology--IM; Histocompatibility Antigens Class II --biosynthesis--BI; Immunoglobulin G--biosynthesis--BI; Immunoglobulin G --immunology--IM; Immunoglobulin Idiotypes--immunology--IM; Immunoglobulin M--immunology--IM; *Interleukin*-*12*--biosynthesis--BI; Lymphoma, B-Cell --immunology--IM; Lymphoma, B-Cell--pathology--PA; Mice; Mice, Inbred C3H; Neoplasm Transplantation; Th1 Cells--immunology--IM

...Chemical Name: Antibodies, Anti-Idiotypic; Antigens; Cancer Vaccines; H-2 Antigens; Histocompatibility Antigens Class II; Immunoglobulin G; Immunoglobulin Idiotypes; Immunoglobulin M; Oligodeoxyribonucleotides; Vaccines, Synthetic; keyhole-limpet hemocyanin; *Interleukin*-*12*; Granulocyte-Macrophage Colony-Stimulating Factor; Hemocyanin

13/3,K/31 (Item 15 from file: 159)
DIALOG(R)File 159:Cancerlit

02470293 98414301 PMID: 9743369

Activation of cutaneous *dendritic* cells by *CpG* -containing oligodeoxynucleotides: a role for *dendritic* cells in the augmentation of Th1 responses by immunostimulatory DNA.

Jakob T; Walker P S; Krieg A M; Udey M C; Vogel J C
Dermatology Branch, National Cancer Institute, Bethesda, MD 20892-1908, USA.

J Immunol (UNITED STATES) Sep 15 1998, 161 (6) p3042-9, ISSN 0022-1767 Journal Code: 2985117R
Document Type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Activation of cutaneous *dendritic* cells by *CpG* -containing oligodeoxynucleotides: a role for *dendritic* cells in the augmentation of

Th1 responses by immunostimulatory DNA.

Genetic vaccination depends at least in part on the adjuvant properties of plasmids, properties that have been ascribed to unmethylated *CpG* dinucleotides in bacterial DNA. Because *dendritic* cells (DC) participate in the T cell priming that occurs during genetic vaccination, we reasoned that *CpG*-containing DNA might activate DC. Thus, we assessed the effects of *CpG* oligodeoxynucleotides (*CpG* ODN) on Langerhans cell (LC)-like murine fetal skin-derived DC (FSDDC) in vitro and on LC in vivo. Treatment with *CpG* ODN as well as LPS induced FSDDC maturation, manifested by decreased E-cadherin-mediated adhesion, up-regulation of MHC class II and costimulator molecule expression, and acquisition of enhanced accessory cell activity. In contrast to LPS, *CpG* ODN stimulated FSDDC to produce large amounts of IL-12 but only small amounts of IL-6 and TNF-alpha. Injection of *CpG* ODN into murine dermis also led to enhanced expression of MHC class II and CD86 Ag by LC in overlying epidermis and intracytoplasmic IL-12 accumulation in a subpopulation of activated LC. We conclude that immunostimulatory *CpG* ODN stimulate DC in vitro and in vivo. Bacterial DNA-based vaccines may preferentially elicit Th1-predominant immune responses because they activate and mobilize DC...

Major Descriptors: Adjuvants, Immunologic--pharmacology--PD; *DNA --immunology--IM; **Dendritic* Cells--immunology--IM; *Dinucleoside Phosphates--immunology--IM; *Oligodeoxyribonucleotides--immunology--IM; *Skin--immunology--IM; *Th1 Cells--immunology--IM

Minor Descriptors: Antigen-Presenting Cells--immunology--IM; Cell Differentiation--drug effects--DE; Cell Differentiation--immunology--IM; Cells, Cultured; DNA--pharmacology--PD; *Dendritic* Cells--cytology--CY; *Dendritic* Cells--metabolism--ME; Dinucleoside Phosphates--pharmacology --PD; Epidermis--drug effects--DE; Epidermis--immunology--IM; *Interleukin*-*12*--biosynthesis--BI; Langerhans Cells--drug effects--DE; Langerhans Cells--immunology--IM; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Oligodeoxyribonucleotides--pharmacology--PD; Skin--cytology--CY...

Chemical Name: Adjuvants, Immunologic; Dinucleoside Phosphates; Oligodeoxyribonucleotides; *Interleukin*-*12*; cytidylyl-3'-5'-guanosine; DNA

13/3,K/32 (Item 16 from file: 159)

02448057 98307293 PMID: 9645386

Bacterial DNA and immunostimulatory *CpG* oligonucleotides trigger maturation and activation of murine *dendritic* cells.

Sparwasser T; Koch E S; Vabulas R M; Heeg K; Lipford G B; Ellwart J W; Wagner H

Institute of Medical Microbiology, Immunology and Hygiene, Technical University of Munich, Germany.

Eur J Immunol (GERMANY) Jun 1998, 28 (6) p2045-54, ISSN 0014-2980 Journal Code: 1273201

Document Type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Bacterial DNA and immunostimulatory *CpG* oligonucleotides trigger maturation and activation of murine *dendritic* cells.

Bacterial DNA and immunostimulatory (i.s.) synthetic *CpG* -oligodeoxynucleotides (ODN) act as adjuvants for Th1 responses and cytotoxic T cell responses to proteinaceous antigens. *Dendritic* cells (DC) can be referred to as "nature's adjuvant" since they display the unique capacity to sensitize naive T cells. Here, we demonstrate that bacterial DNA or i.s. *CpG*-ODN cause simultaneous maturation of immature DC and activation of mature DC to produce cytokines. These events are associated with the acquisition of professional antigen...

... and FACS-fractionated MHC class IIlow (termed immature DC) or MHC class IIhigh populations (termed mature DC) were stimulated with bacterial DNA or

i.s. *CpG*-ODN. Similar to lipopolysaccharide, i.s. *CpG* -ODN caused up-regulation of MHC class II, CD40 and CD86, but not CD80 on immature and mature DC. In parallel both DC subsets were activated to produce large amounts of IL-12, IL-6 and TNF-alpha. *CpG*-ODN-activated DC displayed professional APC function in allogeneic mixed lymphocyte reaction and in staphylococcal enterotoxin B-driven naive T cell responses. We interpret these findings to mean that bacterial DNA and i.s. *CpG*-ODN cause maturation (first step) and activation (second step) of DC to bring about conversion of immature DC into professional APC.

Major Descriptors: *CpG* Islands--immunology--IM; *DNA, Bacterial --immunology--IM; **Dendritic* Cells--immunology--IM; *Oligodeoxyribonucleotides--immunology--IM

Minor Descriptors: Adjuvants, Immunologic; Antigens, CD40--metabolism--ME; Bone Marrow Cells; Cells, Cultured; Enzyme Induction; HLA-B7 Antigen --metabolism--ME; Hematopoiesis; Histocompatibility Antigens Class II --metabolism--ME; *Interleukin*-*12*--biosynthesis--BI; Interleukin-6 --biosynthesis--BI; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Mice, Knockout; T-Lymphocytes, Cytotoxic--metabolism--ME; Tumor Necrosis Factor --biosynthesis...

Chemical Name: Adjuvants, Immunologic; Antigens, CD40; DNA, Bacterial; HLA-B7 Antigen; Histocompatibility Antigens Class II; Interleukin-6; Oligodeoxyribonucleotides; Tumor Necrosis Factor; *Interleukin*-*12*; beta-Galactosidase

?ds

Set	Items	Description
S1	1	(CPG OR CG) (S) (POLYG OR POLY-G OR POLY(G))
S2	6	(ODN (W) 1585)
S3	0	S2 AND (PDC2 OR DENDRITIC)
S4	3	RD S2 (unique items)
S5	277	(DENDRITIC OR PDC2S OR IPCS) AND (CPG OR (ODN (W) 1585))
S6	0	S5 AND (POLY(G))
S7	77	S5 NOT PY>2000
S8	48	RD (unique items)
S9	7	S8 AND (INTERFERON)
S10	7	RD (unique items)
S11	1	S8 AND ((INTERFERON (W) ALPHA) OR (TYPE (W) I (W) INTERFERON))
S12	0	S7 AND (IL-12)
S13	32	S7 AND (INTERLEUKIN-12 OR (INTERLEUKIN (W) 12))

?logoff

19mar04 16:47:45 User259876 Session D601.2

$5.18 1.619 DialUnits File155

$5.88 28 Type(s) in Format 3

$5.88 28 Types

$11.06 Estimated cost File155

$3.00 1.018 DialUnits File159

$4.16 16 Type(s) in Format 3

$4.16 16 Types

$7.16 Estimated cost File159

OneSearch, 2 files, 2.637 DialUnits FileOS

$3.99 TELNET

$22.21 Estimated cost this search

$22.56 Estimated total session cost 2.728 DialUnits

Status: Signed Off. (16 minutes)